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Complete List of Authors:	Quraishi, Mohammed Nabil; University Hospital Birmingham NHS Foundation Trust, Department of Gastroenterology; University of Birmingham, Cancer and Genomic Sciences Widlak, Monika; University Hospital Coventry and Warwickshire, Department of Gastroenterology Bhala, Neeraj; University Hospital Birmingham NHS Foundation Trust, Department of Gastroenterology; University of Birmingham, Institute of Applied Health Research Moore, David; University of Birmingham, Institute of Applied Health Research Price, Malcolm; University of Birmingham, Institute of Applied Health Research Sharma, Naveen; University Hospital Birmingham NHS Foundation Trust, Department of Gastroenterology Iqbal, Tariq; University Hospital Birmingham NHS Foundation Trust, Department of Gastroenterology; University of Birmingham, Cancer and Genomic Sciences
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Systematic review with meta-analysis: the Efficacy of Faecal Microbiota Transplantation for the treatment of recurrent and refractory Clostridium difficile infection

Mohammed Nabil Quraishi [1], Monika Widlak [2], Neeraj Bhala [1,3,4], David Moore [3], Malcolm Price [3], Naveen Sharma [1,4], Tariq H Iqbal [1,4]

1. **Department of Gastroenterology, University Hospital Birmingham, Mindelsohn Way, Birmingham B15 2TH, UK**
2. **Department of Gastroenterology, University Hospital Coventry and Warwickshire, Clifford Bridge Rd, Coventry CV3 2DX, UK**
3. **Institute of Applied Health Research, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK**
4. **Institute of Translational Medicine, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK**

Background:

Clostridium difficile infection (CDI) is the commonest nosocomial cause of diarrhoea. Faecal microbiota transplantation (FMT) is an approved treatment for recurrent or refractory CDI but there is uncertainty about its use.

Aim:

Evaluate the efficacy of FMT in treating recurrent and refractory CDI and investigate outcomes from modes of delivery and preparation.

Methods:

A systematic review and meta-analysis was performed. MEDLINE, EMBASE, CINAHL, Cochrane Library, trial registers and conference proceedings were searched. Studies on FMT in recurrent and refractory CDI were included. The primary outcome was clinical resolution with subgroup analyses of modes of delivery and preparation. Random effects meta-analyses were used to combine data.

Results:

37 studies were included; 7 randomised controlled trials and 30 case series. FMT was more effective than vancomycin (RR: 0.23 95%CI 0.07 to 0.80) in resolving recurrent and refractory CDI. Clinical resolution across all studies was 92% (95%CI 89% to 94%). A significant difference was observed between lower GI and upper GI delivery of FMT 95% (95%CI 92% to 97%) versus 88% (95%CI 82% to 94%) respectively (p=0.02). There was no difference between fresh and frozen FMT 92% (95%CI 89% to 95%) versus 93% (95%CI 87% to 97%) respectively (p=0.84). Administering consecutive courses of FMT following failure of first FMT resulted in an incremental effect. Donor screening was consistent but variability existed in recipient preparation and volume of FMT. Serious adverse events were uncommon.

Conclusion:

FMT is an effective treatment for recurrent and refractory CDI independent of preparation and route of delivery.

Background

Clostridium difficile infection (CDI) is the most important cause of nosocomial diarrhoea usually related to antibiotic use. It is associated with significant morbidity, mortality and cost worldwide.[1] UK National Institute for Health and Care Excellence (NICE) guidelines published in March 2014 recommend the use of faecal microbiota transplantation (FMT) for patients with recurrent CDI that have failed to respond to antibiotics and other treatments.[2] However, a recent survey across England revealed that only just over 25% of hospital trusts perform FMT for this indication. [3] This poor uptake has been attributed by physicians in part to paucity of randomised controlled trial (RCT) data, the lack of a standard treatment protocol, and uncertainty about long-term safety of FMT.[3]

CDI occurs mainly in the elderly and those with significant chronic illnesses.[1] The long-term cure rate from standard first line antibiotics (metronidazole or vancomycin) is low with CDI re-occurring after apparent resolution in about 35% of patients.[4] Recurrent CDI is defined as complete recovery without symptoms followed by at least one further episode of diarrhoea confirmed to be secondary to CDI. Recurrent attacks of CDI expose patients to risk of complications such as toxic dilatation of the colon and septicaemia, which are associated with high mortality. Commonly, tapering doses of vancomycin are used for recurrent and refractory CDI although the effectiveness of this therapy is uncertain with sustained cure rates reportedly ranging widely between 49% and 100%. [5] While fidoxamicin has been shown to be more effective than vancomycin in the resolution of CDI as a first-line agent, this agent has not been tested in recurrent CDI.[6,7]

FMT for the treatment of CDI was attempted first in the modern era by Eiseman et al in 1958 in a small number of patients.[8] Over the past decade or so, FMT has been studied by several centres worldwide for management of recurrent and refractory CDI. However, uncontrolled studies make up the bulk of the supporting evidence. Previous systematic reviews and meta-analyses either have methodological limitations as they have a restrictive selection criteria, do not have a comprehensive search strategy or do not consider the effect of different modalities of preparation or delivery of

FMT. Moreover, they do not include the most recent evidence, which to date includes more than five randomised controlled trials.[9–12] In this systematic review and meta-analysis we therefore aim to address these issues to bring the evidence on FMT in recurrent and refractory CDI up to date.[13,14]

Methods

Objectives

To systematically evaluate the effectiveness of FMT as treatment for recurrent and refractory CDI.

The review and meta-analysis were undertaken in line with guidance from the Cochrane Handbook of Systematic Reviews of Interventions, and reported in line with preferred reporting items for systematic reviews and meta-analysis.[13,14]

Search strategy

The databases MEDLINE, EMBASE, CINAHL, and Cochrane Library were searched from commencement of databases to October 2016 for relevant articles. Free text and index terms for faecal microbial transplantation and Clostridium difficile were combined and no study design or language of publication filters were used. The MEDLINE and EMBASE strategy are shown in Appendix 1. Details of ongoing trials and studies yet to be fully published were sought from trials registers (controlled-trials.com, clinicaltrials.gov), and microbiology, infection, and gastroenterology conferences proceedings (Digestive Diseases Week, British Society of Gastroenterology Conference, United European Gastroenterology Week) from September 2014 to October 2016. Reference lists of existing systematic reviews and articles included in this review were checked for additional studies.

Search results were entered into a bibliography manager and duplicate entries removed.

Study Selection

Titles and abstracts of each article were screened for relevance. Copies of relevant articles were obtained and assessed for inclusion in the review using the criteria below. Screening and selection

were undertaken independently by two reviewers and any disagreements resolved through discussion. The reason for not-selecting studies for review was recorded.

Type of studies:

RCTs, non-randomised trials and case series with 10 or greater participants were included. Studies published in abstract only format (for example from conference supplements) were only included if they were RCTs.

Type of participants:

Studies recruiting patients of all ages with refractory or recurrent CDI were included. Patients include those with ongoing diarrhoea without resolution of symptoms despite standard antimicrobial therapy. Recurrent and refractory CDI was taken as defined by the authors.

Comparator:

For comparative study designs there was no restriction on the type of comparator

Primary outcome:

Studies reporting clinical resolution of CDI based on improvement of symptoms or negative Clostridium difficile stool culture or toxin were included.

Data extraction

Data were extracted using a predesigned collection form on characteristics of study design, participants, type of CDI (recurrent and/or refractory) and outcomes. In addition data were extracted on donor screening, procedural aspects (FMT preparation, pre-medications and number of infusions) to establish variation of practice. Data on adverse events were also collected.

There was no missing data or unclear information that necessitated contacting study authors for clarification. For papers not published in English partial translations were undertaken (in one case).

Data extraction and risk of bias assessment were undertaken by two reviewers independently. If there were any discrepancies, a third reviewer was consulted (in one case).

Risk of Bias

RCTs were assessed with the Cochrane Collaboration's risk of bias tool.[13] For non-randomised trials the same tool was to be used without application of criteria related to randomisation. Case series were assessed using the Centre for Reviews and Dissemination guidance.[15]

Data assessment and analysis

The effect of FMT on clinical resolution of recurrent and refractory CDI was evaluated by analysing studies with direct comparison against a non-FMT arm. The overall effect of FMT was analysed using data from all studies (including the FMT arm data from RCTs).

The author's definition of outcome of CDI resolution was used at the time point specified by the author following the delivery of FMT. In order to study the effect of multiple infusions, the data was analysed to compare rate of clinical resolution if only a single infusion was administered and if more than one infusion was delivered.

Analysis was carried out to study the effects on FMT efficacy of mode of FMT delivery (upper GI (foregut) versus lower GI (colonic)) and different preparations of donor stool (fresh versus frozen). These comparisons were performed first with RCTs (if any) and then on subgroups of case series for each assessment. As it was anticipated that studies on the whole would not clearly differentiate between patients with recurrent and refractory CDI, no separate analyse on these subgroups was undertaken. A descriptive analyses of adverse event data was performed.

Statistical analysis

For the primary outcome pooled estimates of relative risk from the RCTs, and response rates from case series, were estimated with a random effect model using the method of DerSimonian &

Laird.[16,17] For the latter the pooled estimate was calculated after the Freeman-Tukey Double Arcsine Transformation was applied to stabilise the variances facilitating synthesis of studies with 100% response rate.[18] Exact confidence intervals were calculated for the individual studies.

Heterogeneity was assessed using the I^2 statistic and calculation of 95% prediction intervals for the response proportion in a new study.[19,20] The latter were calculated using a logistic regression model with a random intercept. In interpreting I^2 we describe values from 0%-30% as being likely minimal, values from 30-60% as likely moderate, and values from 60%-100% as likely substantial heterogeneity. The possibility of small study effects was assessed by asymmetry of funnel plots if 10 or more studies contributed to a meta-analysis and the potential impact quantified using the Duval and Tweedie nonparametric "trim and fill" method.[21]

Confidence intervals for relative risks from individual RCTs were calculated assuming the sampling distributions of the log-relative risk are normally distributed. All analyses were performed in STATA version 14.

RESULTS

Study characteristics

The initial search identified 2097 publications. Of these, 1179 duplicates were excluded and an additional 615 were removed after screening titles and abstracts. Consequently, 303 papers were retrieved in full text. Of these 19 were systematic reviews from which no additional papers were identified. From the remaining 284 papers, 102 were overviews, summaries, opinion pieces and narrative reviews, 83 were case reports or case series with a sample size of less than 10 patients and 62 were case series published only as an abstract. Therefore 37 papers reporting studies met the selection criteria (Figure 1).

The 37 included studies are summarised in Table 1 and Supplement 1. Supplement 1 elaborates on the primary response rate data and assessment of study quality. Seven studies were RCTs (of which

two were only published in abstract form) and 30 were case series. The different arms of the RCT data are summarised in Table 2. The included studies included a total of 1973 patients with 428 enrolled in RCTs (360 in the donor FMT arm and 68 in the non-donor FMT arm) and 1545 described in case series. Two RCTS were open label comparisons of vancomycin and FMT (van Nood et al and Cammarota et al).[22,23] Both were ended early following interim analysis by the respective data and safety monitoring boards due to observed efficacy of FMT. One RCT compared autologous versus donor FMT (Kelly et al), and the remaining RCTs compared different forms of FMT or modes of delivery: Fresh and frozen FMT (Lee et al), capsule versus colonoscopic delivery (Kao et al), low dose versus high dose FMT (Allegretti et al), nasogastric versus colonoscopic delivery (Youngster et al).[24–28]

Of the case series, 25 performed FMT solely using fresh stool, two studies solely used frozen stool, two studies performed FMT with both fresh and frozen and one did not report on FMT preparation. Eight studies delivered FMT via the upper GI route, 18 studies delivered FMT via the lower GI route and one study delivered FMT via both routes. The remaining studies used a combination of both routes but did not report on data separately. Almost all the 30 studies had similar cohorts with regard to age and gender and similar response rates were observed in older and younger groups and those with male or female predominance as shown in Table 1 and Supplement 1. There was a female preponderance in the studies with a male: female distribution of 2:3. No studies solely used toxin negativity to define clinical resolution. Prior endoscopic evaluation was undertaken in six studies.

Donor screening protocol

Donors were a mixture of spouses, intimates, relatives and healthy volunteers. Most studies used a screening procedure to exclude individuals with known exposure to transmissible viruses, sexually transmitted disease, those involved in high-risk sexual behaviours and those with a history of drug abuse. Those with known gastrointestinal co-morbidity were excluded as were those who had recently taken antibiotics. With regard to donor screening there was considerable standardisation in screening for blood-borne viruses with screening for common transmissible agents such as hepatitis

A, B, C, HIV 1&2, *Helicobacter pylori* and Treponema in blood. This also applied to stool pathogens including *Clostridium difficile* toxin, common pathogens including *Cryptosporidium* and *Giardia* and the majority of studies also reported microscopic examination for ova, cysts and parasites in stool samples.

Procedural aspects

i) FMT preparation

In eight studies the solvent was water, saline in 20 and glycerol was used as a cytoprotectant in the three studies using frozen stool preparations. The remaining studies did not describe the diluent used to make up the transplant material. Where stated, time from collection to administration varied from 1 hour to 8 weeks for frozen stool whilst the median time was six hours for studies using fresh stool samples. Quantity and volume of FMT material was very variable. In the studies using the upper route of delivery, the volume of material varied from 25ml to 500ml and the mass of faecal material also varied widely from 6g up to about 140g (median 40g). In the studies reporting on the lower GI route of delivery the volume of FMT was reported in 19 and this ranged from 100ml to 1000ml with a mean volume of about 450ml. The fresh mass of faecal matter used was variably reported from 30g to 152g (median of 86g). Two RCTs used capsulated forms of stool however further details on the preparation of these capsules was not available as the data was only published in an abstract form.[26,32]

ii) Pre-medication

Standard colonoscopy bowel preparation was used in all studies undertaking FMT via the lower GI route. Proton pump inhibitors were given in most studies using the upper route with the exception of the Van Nood randomised controlled trial.[22] The use of anti-diarrhoeals to prolong retention of the faecal suspension in the colon was also reported in two studies. Antibiotics were generally

stopped 1-2 days before FMT with the exception of the van Nood RCT where antibiotics were continued until the day of the treatment.[22]

iii) Number of infusions

24 studies allowed more than one infusion / treatment of FMT in the event of failure of response. Of the 13 studies that only performed a signal infusion of FMT 9 were done using the lower GI route, 3 used only the upper GI route and one used either route.[26,27,33–43] Twelve studies used only fresh stool, and one used either fresh or frozen and 1 performed FMT also using a capsulated form. In the remaining studies FMT was administered up to 4 times for recurrent or unresolved symptoms.

Assessment of study quality

The seven RCTs were assessed to have a low risk of bias and demonstrated adequate randomisation with concealed automated allocation and performed an intention to treat analysis. For case series, although selection criteria were defined in most of these studies, all mentioned or implied consecutive recruitment of patients. Patients were followed up till achievement or failure of the primary outcome. Consequently, few studies reported long term outcomes and adverse events. Follow up ranged from 10 weeks to 8 years.

Efficacy of FMT

Most studies differed in their definition / criteria for resolution of CDI. Hence the author's definition of outcome of CDI resolution at their specified time point following the delivery of FMT was used. Based on the variability of definitions used in the literature it was not possible to clearly separate data on "recurrent" versus "refractory" CDI. There were no true placebo controlled trials investigating the efficacy of FMT.

<u>Response to FMT - RCTs</u>

There were 3 RCTs that compared FMT to a non-FMT intervention. In the two RCTs comparing FMT to vancomycin, the pooled relative risk of treatment failure of FMT against vancomycin was 0.23 (95% CI 0.20 to 0.80) with moderate heterogeneity (I^2 = 41%) indicating the superiority of FMT.[22,23] The relative risk against vancomycin and bowel lavage in the RCT by Camorotta et al was 0.08 (95% CI 0.01 to 0.05).[23] The overall response rate from the two RCTs comparing FMT to vancomycin was 90% in the FMT arm while the response rate was less than 30% in the antibiotic arms. The RCT by Kelly compared single infusion of donor versus autologous FMT.[27] In the intention-to-treat analysis, 20 of 22 patients (90.9%) in the donor FMT group achieved clinical cure at 8 weeks compared with 15 of 24 (62.5%) in the autologous FMT group (P = 0.042).

The RCT by Lee and colleagues (comparing fresh versus frozen FMT) reported an overall combined clinical resolution rate with FMT of 72% in the intention-to-treat analysis, and 84% in the per protocol analysis across both arms.[24] This was 52% for a single infusion but increased to 96% in patients who received more than two FMTs in the 13 week period. The RCT by Youngster (comparing nasogastric versus colonic FMT) reported a primary response rate (one infusion) of 70% across both arms and this increased to 90% with a second infusion in those that failed to respond to the first.[28] A further two RCTs published in abstract form comparing efficacy with capsule versus colonic delivery and low dose versus high dose capsulated FMT both showed a response rate of 95% across both FMT arms.[26,32] Kao demonstrated a cure rate of 100% versus 92% in colonoscopy and capsule delivered FMT respectively.[26] In the Allegretti study presented at the Digestive Diseases Week in San Diego 2016, the authors reported on encouraging remission in 14 out of 19 patients treated with either a low or high dose of capsules.[32] The abstract reports the 5 non-responders at 8 weeks were all given a high dose of capsules with cure in 4.

Response to FMT – all studies

The mean pooled overall response for FMT in recurrent and refractory CDI based on all the included 37 studies regardless of the number of infusions was 92% (95% CI 89% to 94%) with likely moderate heterogeneity (I^2 = 59%) (figure 2). From the 34 studies that presented efficacy data for a single FMT infusion, the mean pooled response rate was 84% (95% CI 79% to 89%) with a likely high degree of heterogeneity (I^2 = 84%). For a single infusion a 95% prediction interval for the response proportion in a new study is 49% to 96%. On analysis by funnel plot, studies were not symmetrically distributed about the pooled estimate possibly indicating an absence of some smaller and medium sized studies with findings that, although favourable, are not as favourable as other small studies. There are many possible reasons for this including chance, small study effects and publication bias. When this funnel plot asymmetry was adjusted for, the efficacy of one or more FMT infusions was only reduced by a small amount to 79% (95% CI 73% to 84%) (supplement 2).

The case series had cure rates ranging from 68 – 100% with only one study having an overall response rate of under 75% and eight case series demonstrating a response rate of 100% (although there was incomplete follow up in some of these studies).

Only one study addressed the efficacy of FMT for treatment of CDI in immunocompromised patients. [30] This study included a series of patients with IBD, solid organ transplants on immunosuppression, HIV and cancers. The CDI cure rate observed after a single FMT was 78%, with an overall cure rate of 89% following a second transplant.

Comparison between upper GI and lower GI routes of delivery

The RCT that compared nasogastric (upper GI) versus colonic delivery of FMT reported a cure rate of 60% at 8 weeks with a single infusion and an overall cure rate 80% after second infusion when delivered via NG.[28] The cure rate with colonic delivery was 80% with a single infusion at 8 weeks and an overall cure rate of 100% after a second infusion.

Of the remaining studies, 25 case series and 7 RCTs had separate outcome data for modes of FMT delivery. 22 delivered FMT by the lower GI route (colonoscopy or retention enema) and 11 delivered FMT by the upper gastrointestinal route (upper GI endoscopy, nasogastric tube or naso-jejunal tube). Results are displayed in figure 3. The pooled response of CDI to lower GI-delivered FMT was 95% (95% CI 92% to 97%) with likely moderate heterogeneity between the studies (I^2 = 48%). When adjusted for funnel plot asymmetry overall response was 90%. This compared to the overall pooled response rate to upper GI FMT of 88% (95% CI 82% to 94%) with moderate observed heterogeneity between the studies and adjusting for funnel plot asymmetry revealed a response rate of 83%. There was evidence of a difference between the delivery methods with respect to response to FMT (p=0.02). Analysis of cure rate with a single infusion did not show a significant difference with route of delivery with a response of CDI of 81% (95% CI 73% to 88%) to lower GI-delivered FMT and of 87% (95% CI 79% to 94%) for upper GI-delivered FMT (p=0.20).

Comparison of freshly prepared versus frozen FMT

In the RCT by Lee patients received either FMT prepared no more than five hours earlier (n=111) or FMT frozen for up to 30 days (n=108).[24] The clinical resolution of diarrhoea using intention to treat analysis showed no evidence of a difference in outcome between preparations, with a relative risk of failure to respond of 1.19 (95%CI 0.77,1.84) with a 70% response in the fresh FMT group and 75% in the frozen FMT group. This increased to 85.6% and 90.7% respectively when patients were given multiple infusions FMT due to lack of response.

Of the other studies, thirty case studies used fresh stool and 4 studies (2 case series, 2 RCTs) used frozen stool to prepare FMT and a response rate was calculable for each group. For the fresh FMT studies the overall response rate was 92% (95% CI 89% to 95%) with moderate heterogeneity between the studies (I^2 = 54%). When adjusted for funnel plot asymmetry the overall response rate was 87%. The overall response in frozen FMT studies was 93% (95% CI 87% to 97%) with minimal observed heterogeneity between the studies (I^2 = 19%). There were insufficient studies to assess

funnel plot asymmetry. There was no evidence of a difference in response between the two groups (p=0.84) (figure 4). Analysis of a single infusion revealed a response rate of 85% (95% CI 79% to 90%) for fresh FMT and a lower response rate of 68% (95% CI 47% to 86%) for frozen FMT but there was only very weak statistical evidence of a difference (p=0.10)..

Adverse Events

The RCT by Van Nood reported no significant adverse events (SAEs) in 16 patients treated with FMT, however there were two urinary tract infections and one patient suffered from choledocholithiasis. [22] No SAEs related to FMT were reported in other RCTs. Transient mild diarrhoea and cramping was very common in the FMT arm of three RCTs by Lee, Cammarota, Van Nood, and about 25% of the recruits in the RCT by Lee reported long term constipation and flatulence following FMT. Similarly, 19% of patients in the FMT arm reported constipation in follow up period in the van Nood RCT. Mild abdominal pain and bloating was reported in 20% of patients treated by a frozen inoculum of FMT.[28] In the RCT by Kelly et al comparing FMT with autologous vs heterologous (donor) stool administered by colonoscopy, chills were observed more frequently in autologous group.[27] Rates of other minor AEs did not differ significantly between groups.

In the case series most side effects were minor and often transient: bloating, belching, abdominal cramps, pain or discomfort, nausea, vomiting, excess flatulence, constipation, transient fever, urinary tract infections, self-limiting diarrhoea, and irregular bowel movement. However, recurrent and refractory CDI negative diarrhoea or worsening diarrhoea following FMT was also reported although the duration of this adverse event was not reported.[37,44] The data from these case series did not allow an assessment of any differences in adverse events by route of treatment or use of fresh or frozen transplant.

There were no reported cases of aspiration following FMT delivery via the upper GI route. In one case the patient vomited immediately after FMT application via nasogastric tube.[45] There was only

one reported case of mucosal tear and micro perforation following colonoscopic delivery of FMT.[30,46] Hospitalisation with self-limited FMT related abdominal pain, was reported in one patient.[30]

There were 50 deaths reported in the studies reviewed, however these were almost all due to critical illness of elderly patients with multiple comorbidities or unrelated illness and were not directly attributed to the FMT. However, there was a death as a result of aspiration at the time of sedation for the colonoscopy to administer the FMT.[30] Two patients with recurrent diarrhoea and initial response to the FMT died subsequently from complications of ileus and colonic perforation Four deaths in patients infected with the ribotype 027 strain who did not respond to FMT and died within 3 months were also reported.[47]

Of note, a case series of FMT in 80 immunocompromised patients with three month follow up did not report any serious adverse events.[30] However, four patients with inflammatory bowel disease experienced a flare up of their condition after FMT. Similarly a case series of 146 elderly patients that were followed up for one year did not report any serious adverse events.[48]

DISCUSSION

This systematic review and meta-analysis has demonstrated that FMT is a highly effective treatment for resolution of recurrent and refractory CDI. Even the most conservative analysis gives an estimate of efficacy of a 49% response rate for FMT in this setting based on the lower prediction interval for a single infusion. Previous systematic reviews and meta-analysis have reported the marked efficacy of FMT for treatment of CDI in the range of 88 to 92%, similar to our findings.[9,10] These, however, pre-dated or failed to include the five recent RCTs and included far fewer case series.[23,24] There is good agreement between the efficacy demonstrated in observed response rates in the seven RCTs (only three of which have a non-FMT comparator arm) performed to date and the reports from case

series. The limited data on mortality and significant adverse events suggests that FMT is safe and generally well tolerated, even in sick immunocompromised elderly patients.[30]

No previous meta-analysis has compared fresh and frozen FMT in treatment of recurrent CDI, whilst the present study shows no difference in efficacy between these modes of stool preparation. The review also demonstrates that repeated infusions of FMT in non-responders resulted in a higher cure rate albeit with some limited data for this analysis. Previous reviews have suggested that the efficacy for lower GI route is greater than upper GI route (Kassam et al, (91% vs 80% respectively (p=0.046)).[10] We have however shown that this difference was no longer significant when efficacy with only a single infusion was analysed.

With regard to attempting to differentiate between the efficacy of FMT for recurrent or refractory CDI, we found that the distinction between recurrent and refractory disease in the case series is often vaguely reported and not robust enough to allow for meaningful sub-group analysis. Similarly, previous reviewers have reported that no studies have compared refractory CDI to standard therapy and from the small numbers of patients being treated for solely refractory CDI meaningful analysis is difficult.[11,12]

This systematic review and meta-analysis is a comprehensive ascertainment of the available evidence through a detailed search strategy, and includes the seven RCTs to date. Structured analyses were performed to address key issues with regards to storage and administration of FMT that may improve wider uptake of this treatment strategy. There are, however, limitations to our analysis. Characterisation of initial /primary response depended on the authors' definitions, hence varying between studies and being sometimes poorly defined. Although almost all studies defined initial response as resolution or improvement of diarrhoea, but the time to response varied from 1 day to 90 days and the overall response varied from 7 days to 3 months. Most studies failed to report *C. difficile* toxin for assessment of clearance in several studies lacked long-term data. A recent paper has highlighted the high incidence of IBS after an attack of CDI.[48] There was significant

variability of dose of FMT and several studies defined their clinical resolution following use of more than one infusion of FMT. The use of concomitant medications and other biases may be greatly underestimated given the retrospective nature of most of the case series included in this review.

The data suggest that, irrespective of route of delivery or method of preparation repeated treatments have an incremental benefit. There are no clear strategies for this and guidelines are required, as well as additional RCTs to further determine the optimal dose and long-term outcomes and side effects of FMT are required. Finally, 'corrected' estimates calculated using the Trim and Fill method should be treated with great caution and as indicative as the method does not take into account reasons for funnel plot asymmetry other than publication bias and limited numbers to detect differences in subgroup analyses.[13]

Included studies exhibited substantial heterogeneity in procedural aspects of FMT preparation and delivery. Donor screening appeared to be robust and studies consistently had strict exclusion criteria based on history of high-risk behaviours, recent antibiotic use and a comprehensive serology of blood borne viruses and stool cultures for pathogens. FMT was prepared using water or saline along with glycerol in most studies. However the quantity and volume of stool and solvent used to prepare the transplant was very variable.

Patients who underwent FMT via a lower GI route received a larger amount / concentration of FMT compared to those who had it delivered via the upper GI route. The number of infusions prior to achieving clinical resolution as defined by the authors also varied significantly between studies although most studies only gave a single infusion. There is little uniformity of practice with regard to treatment protocol with respect to the triggering of subsequent treatments after the first.

This review is focussed on FMT and, as such, we have not included emerging data from investigations using faecal bacteriotherapy in which the microbiota is altered or in which specific bacteria are infused.[49,50]

Short-term adverse events were reported in almost all the studies however there was lack of consistency in long-term follow up for adverse events in uncontrolled studies and this was often reported on an ad-hoc basis. Follow up was also limited to 10 -13 weeks in RCTs. Most adverse events were self-limiting gastrointestinal symptoms including abdominal cramps, constipation, diarrhoea and usually occurred within 24 hours of the procedure and resolved within a week of the FMT. Deaths reported following FMT were almost always due to inter-current illness unrelated to CDI, FMT and overt failure to respond to FMT. On the whole the current evidence suggests a good short-term safety of FMT however data is limited and uncertainty remains concerning unrecognised long-term consequences. It should also be noted that in this review studies were selected based on whether they reported an outcome related to resolution of CDI and that case series with less than ten patients were not analysed. Thus it could be argued that this review is not comprehensive of all studies that might report adverse events.

Despite uncertainty FMT for the treatment of CDI associated colitis has been adopted as the biological rationale for its use is compelling and the treatment is cheap. The second line antibiotic treatment for CDI associated colitis after standard antibiotics (metronidazole and vancomycin) is fidaxomicin and this is vastly more expensive than FMT.[1] Moreover, there is no current evidence for fidaxomicin in the treatment of recurrent CDI and as yet no direct comparison of the effectiveness of this antibiotic against FMT.

In the UK NICE has approved FMT “for patients for with recurrent CDI that have failed to respond to antibiotics and other treatments”. [2] However, despite this official stamp of approval, standards of governance with respect to the procedure itself remain undefined. This is perhaps particularly pertinent now that manipulation of the microbiome is being considered in younger cohorts of patients for indications other than CDI associated colitis.[51,52]

Most studies appear to comply with the donor screening criteria outlined by the American Gastroenterology Association.[53],[54] However there is no agreement as to what constitutes an

acceptable donor with respect to, for example, relatedness to the patient, lifestyle, diet, co-morbidity, body mass index and there is no mandate with regard to follow up of donors. Similarly no consensus exists about fundamental aspects concerning the actual process of delivering FMT. Some investigators use the upper GI route for the administration of FMT others (the majority of published studies) use colonoscopy or retention enemas. There is little evidence of uniformity with respect to stopping other treatments prior to FMT or concomitant treatments to be used to facilitate FMT. However despite a lack of consistent approach the clinical efficacy for FMT is universally positive and much greater than that seen with antibiotics. A recent International Consensus has highlighted the uncertainties concerning route of delivery, donor selection (household members/healthy volunteers), the place of routine pre-treatment with antibiotics and bowel preparation and, in light of long term safety concerns, the desirability of establishing a patient registry. [55]The utility of frozen FMT has gained significant interest as it allows the ability to deliver treatment on demand and to a wider population. As a result recent regulatory discussions concerning FMT provision in the European Union have led to the situation that FMT use in the context of clinical trials is to be controlled by regulatory authorities.[56]

Data is beginning to emerge regarding the association of microbiome alteration with response to FMT. In a recent study from the US, the authors reported specific gut microbiota signatures associated with response to or recurrence after FMT.[57] This raises the possibility of predicting which patients may not respond to primary treatment with antibiotics and those then likely to need FMT. In another intriguing study from this group it was reported that microbiota changes associated with bile salt metabolism following FMT may also indicate patients likely to progress to recurrent CDI and the need for FMT.[58]

In the future it is likely that we will see further data emerging from investigators who prepare "designer" FMT or by culturing specific organisms in vitro particularly as we better understand

microbiota profiles which differentiate health from disease and the profile which is associated with successful FMT.[49,50]

In conclusion, FMT appears to be an effective and possibly a safe treatment strategy for recurrent and refractory CDI. The efficacy is similar in both controlled and uncontrolled studies. The current data is relatively heterogeneous with regards to the methodology for transplantation and the outcome measure for resolution of CDI. Whilst this could be explored with the current evidence base to refine estimates and potentially suggest effect modifiers, the effect of FMT on resolution of recurrent/refractory CDI markedly evident and appears to be quantitatively in excess of that seen with other antimicrobial therapies such as vancomycin. Further studies should be of robust design and focus on determining the optimal procedures and long-term outcomes and side effects of FMT in order that FMT is available to help alleviate the burden of this significant iatrogenic hazard.

Figure 1. Flowchart of search

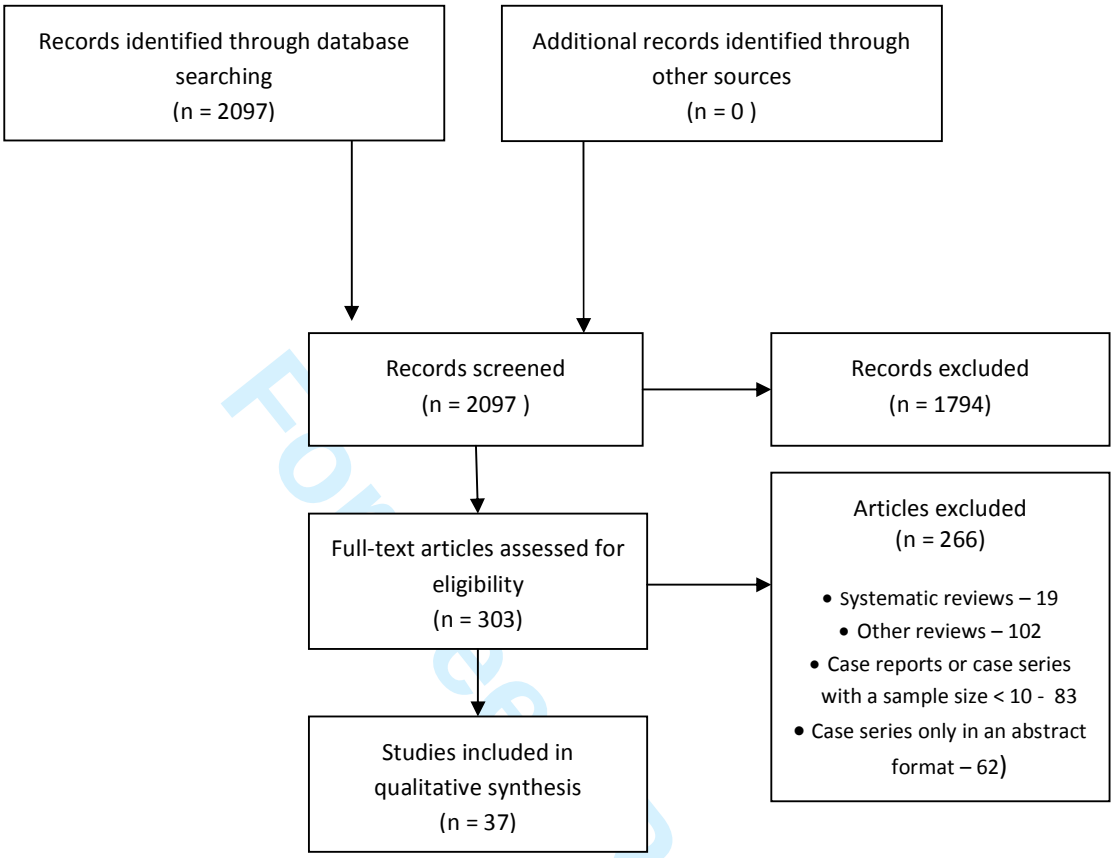
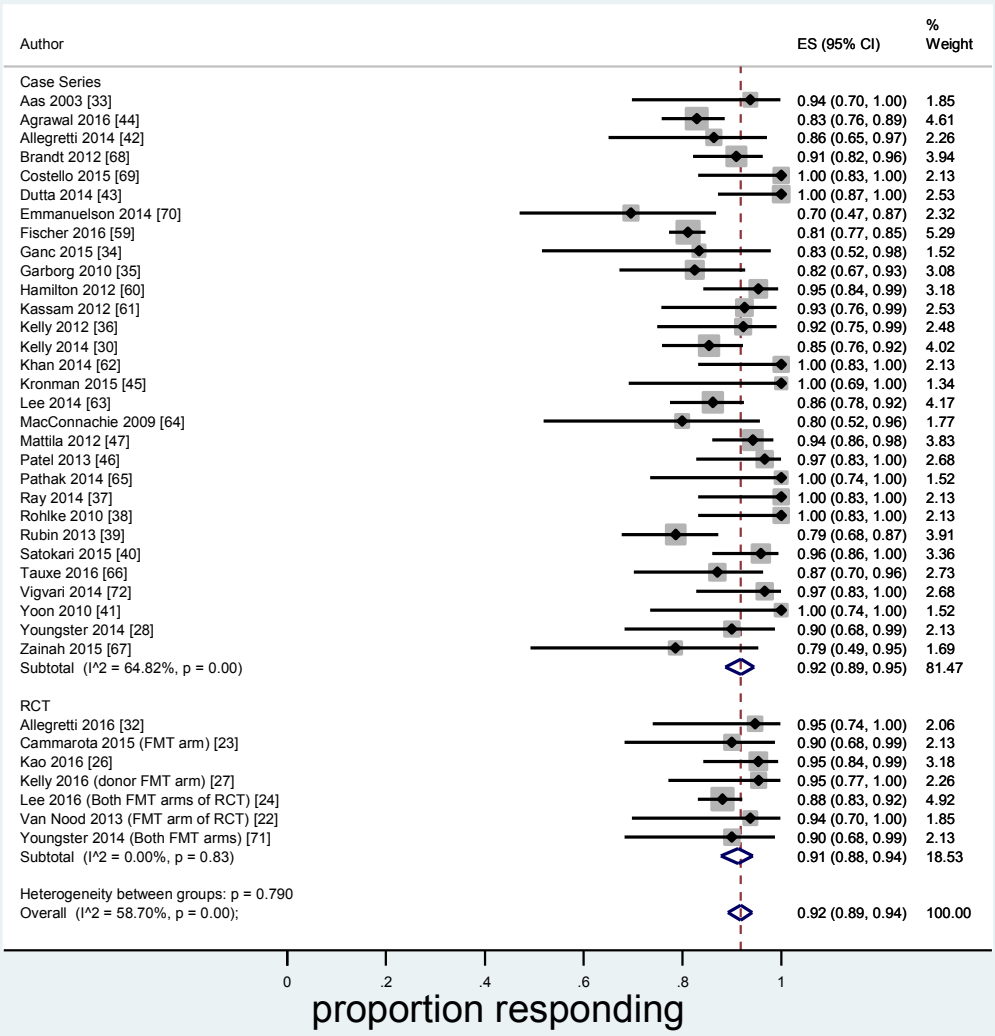


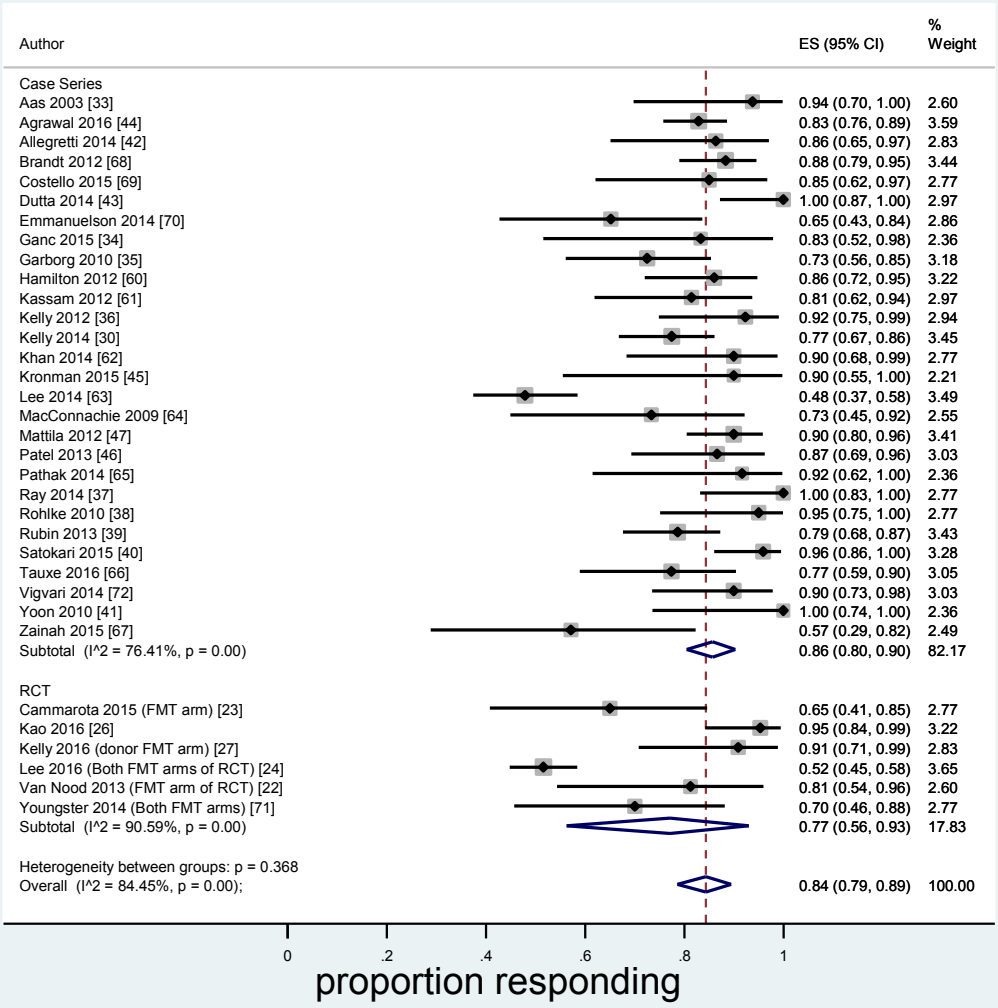
Figure 2 Forest plot of the proportion responding to treatment for all included studies

a) Multiple infusions



ES (95% CI) is the proportion responding with its 95% confidence interval.

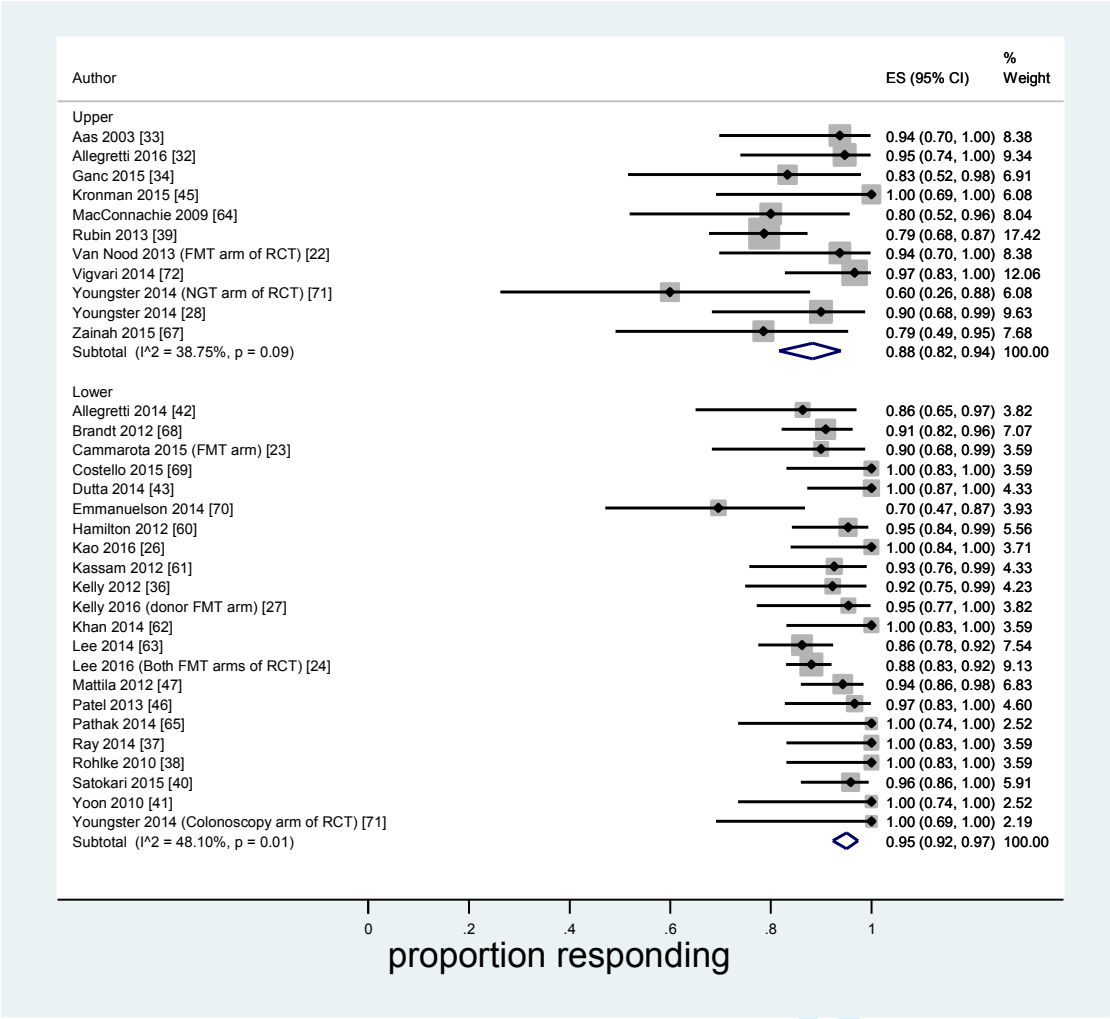
b) Single infusion



ES (95% CI) is the proportion responding with its 95% confidence interval.

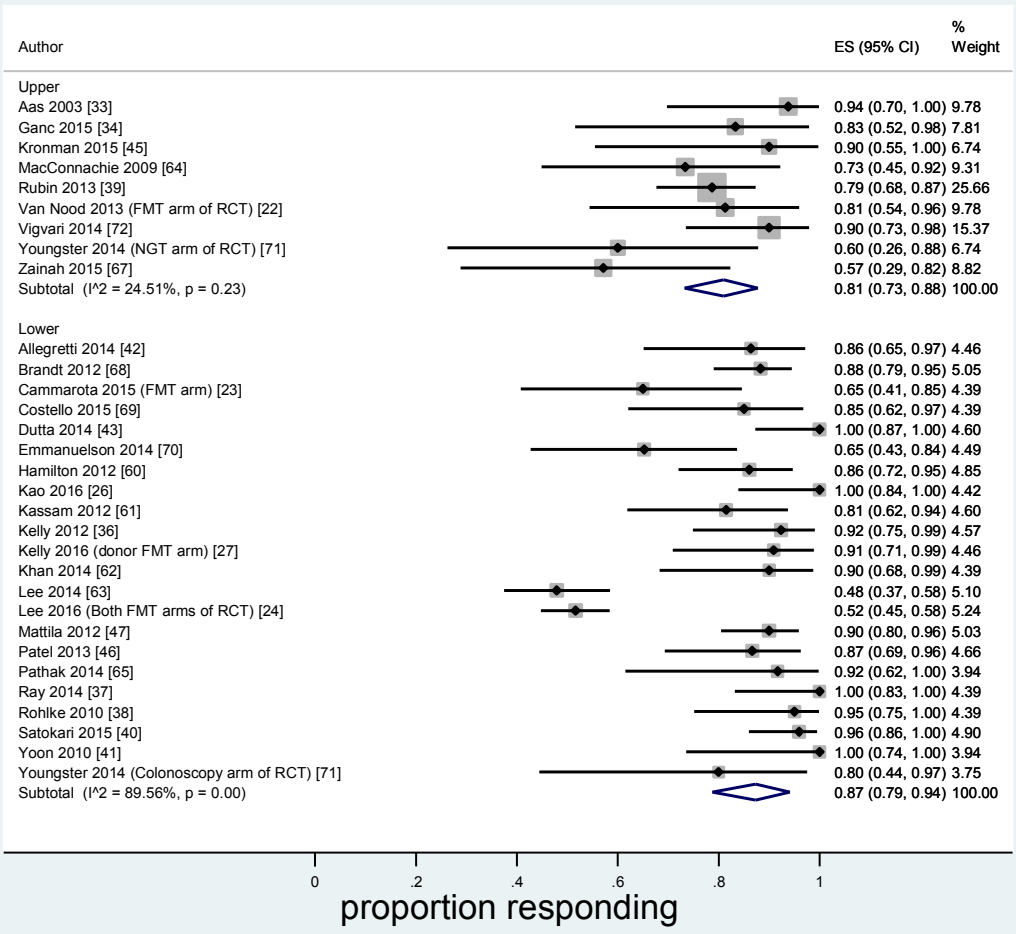
Figure 3. Forest plot of the proportion responding to treatment by Upper GI ad Lower GI routes of delivery.

a) Multiple infusions



ES (95% CI) is the proportion responding with its 95% confidence interval.

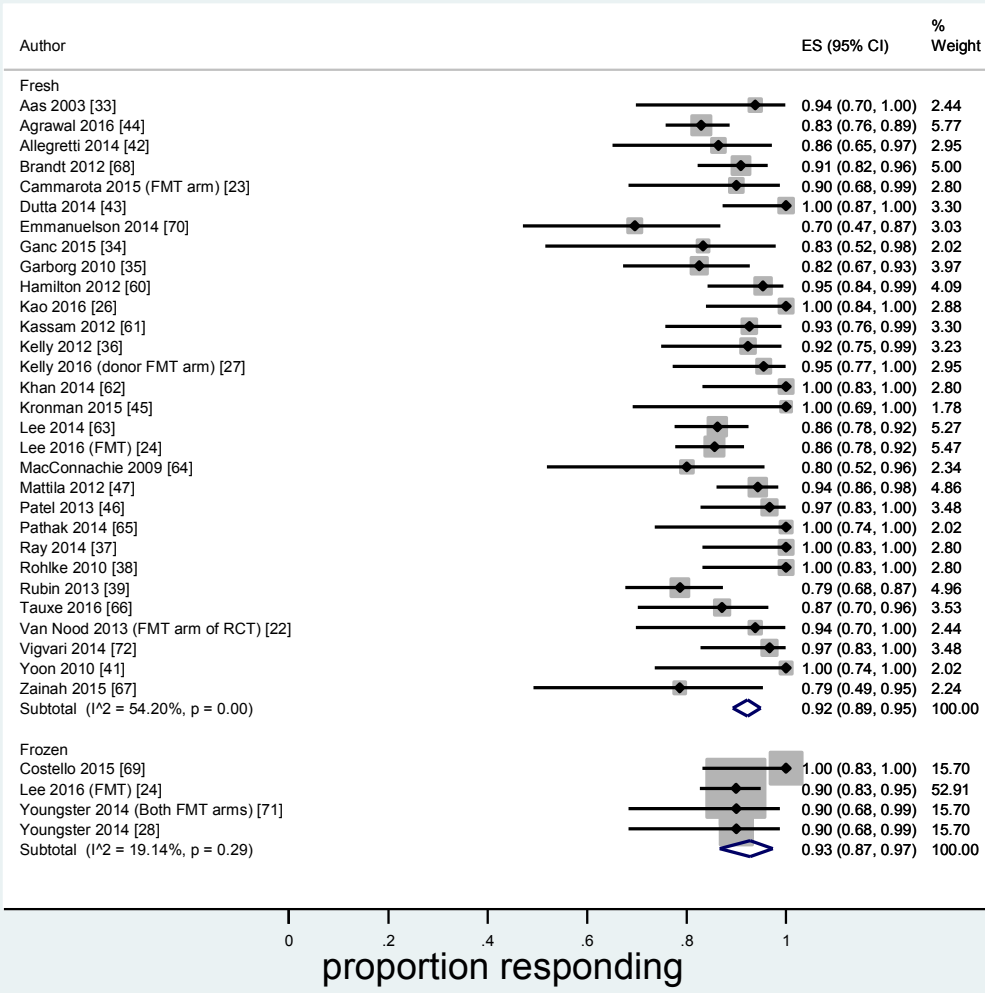
b) Single infusion



ES (95% CI) is the proportion responding with its 95% confidence interval.

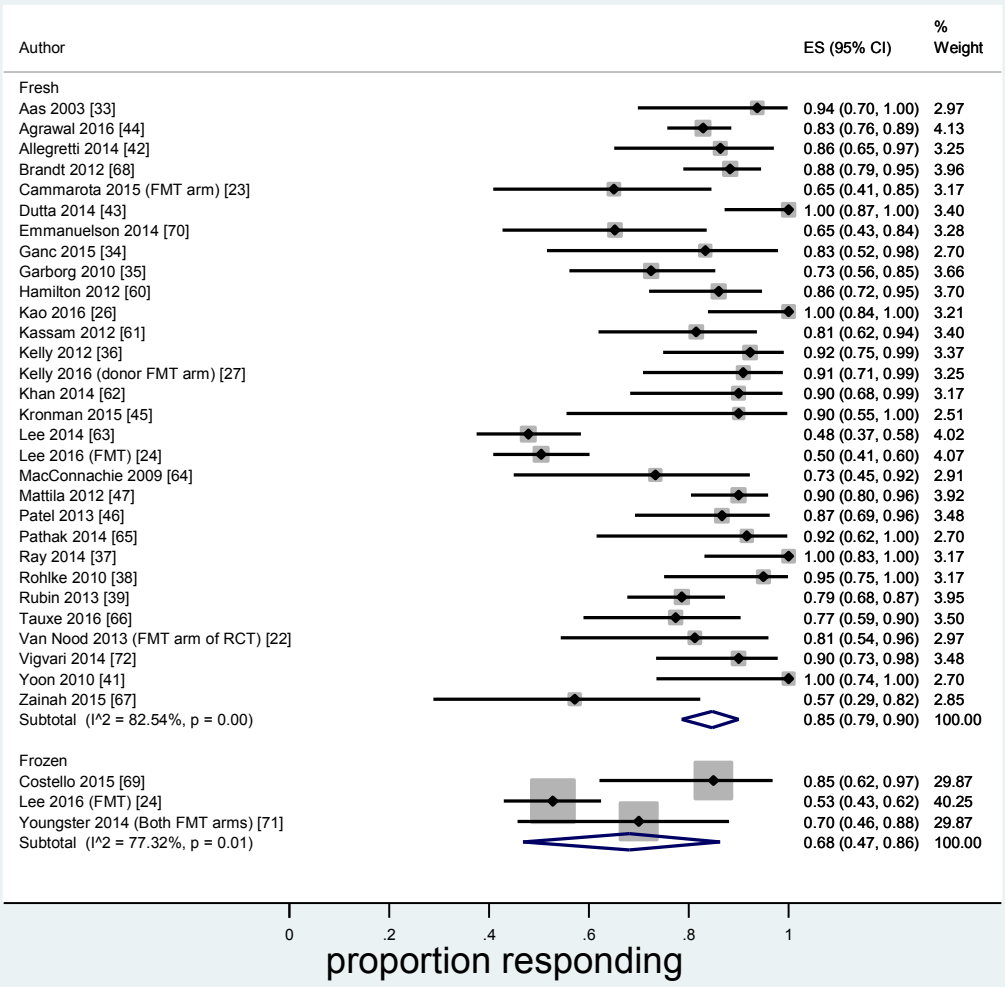
Figure 4. Forest plot of the proportion responding to treatment by freshly prepared versus frozen FMT.

a) Multiple infusions



ES (95% CI) is the proportion responding with its 95% confidence interval.

b) Single infusion



ES (95% CI) is the proportion responding with its 95% confidence interval.

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Statement of Interests

We have read and understood AP&T policy on declaration of interests and declare that we have no competing interests.

Authorship statement

TI received a commission from APT in 2015 to undertake a systematic review and meta-analysis of the literature concerning the efficacy of FMT in treating CDI. TI conceived and designed the review. DM, MNQ, MP developed the review protocol. MNQ and TI performed eligibility screening, carried out the data extraction and methodological quality assessment. MNQ, TI, NS and MW provided advice and arbitration on the selection process, data extraction and methodological quality assessment. MNQ, NS, MW and TI analysed the data. DM and MP interpreted the data. MNQ, TI, NS and NB wrote the original draft, and all authors revised the draft critically for important intellectual content and approved the final version of the paper, including the authorship list.

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Study details			
Name, Year	**Type of study i.e RCT, case control etc**	**No. of patients, years, location, selection criteria, Mean or median age, Gender distribution; other**	**Diagnosis of C.diff i.e Elisa/PCR, duration from diagnosis to transplant**
Aas 2003	Case series	19 recruited over 9 years (1994-2002) at a single centre (USA); two or more lab confirmed relapses after initial specific AB treatment, adequate clin and lab documentation of post transplant course; Mean age 73±9 (SEM) (Range: 51-88 years); F: 13/18 (72%); Hospitalised=5; nursing home=3; outpatient-GI clinic=10)	Lab confirmed via stool sample, toxin A only, then B added from 2001. 2 or more positive test stool tests (mean 3.2, range 2-7). Mean period from diagnosis of c/diff colitis and stool transplantation 102±24 (SEM) days (range 25-497)
Allegretti 2016	Open label cluster dose finding trial comparing low dose (30 pills) vs high dose (30 pills on 2 consecutive days)	19-age/gender not stated	Diagnosis method not stated
Cammarota 2015	Open label RCT	prospective RCT comparing FMT plus vancomycin to vancomycin therapy alone for recurrent CDI; 39 patients over 12 months July 2013 to June 2014; single centre; FMT group (n=20) mean age 71 years (range 29-89) F 12 (60%); Vanc group (n=19) mean age 75 (49-93) F 11 (58%)	CDI diagnosis was based on symptoms and toxin confirmed in 23/39(59%) positive ulture.mean duration of CDI diagnosis prior to FMT not stated
Fischer 2016	Retrospective cohort study	Of 328 patients in the developmental cohort, 73.5% (N=241) were females with a mean age of 61.4±19.3 years; 19.2% (N=63) had inflammatory bowel disease (IBD), and 23.5% (N=77) were immunocompromised. Two academic centres. 2011-2015. Of 134 patients in the validation cohort, 57% (N=77) were females with a mean age of 66±18.1 years; 9.7% (N=13) had IBD, and 17.9% (N=24) were immunocompromised. Single centre. 2011-2015	Diagnosis of Cdiff if recurrent at least 3 episodes of CDI and failure of 6-8 week vancomycin taper. Severe based on albumin, elevated white cell count and abdominal pain. Severe complicated defined as admission to ITU hypotension, fever, ileus, reduced GCS, elevated white cell count and lactate with end organ dysfunction.

Ganc 2015	Case series, retrospective	12 patients. No other variables reported	Not reported
Garborg 2010	Case series, retrospective	39 patients (one had 2 FMTs). Treated single centre 1994-2008. Mean age 75y (range 53-94). F=21 (53%)	Toxin positivity or clinical findings (37/40 toxin positive)
Hamilton 2012	Case series	43 patients. Single centre. 29 non-IBD and 14 IBD patients. Non IBD cohort (mean age 64.7y SEM 3.3; F 20 (69%)); IBD cohort (mean age 44.6 SEM 5.8; F 11 (79%))	Inclusion criteria for FMT included a history of symptomatic, toxin-positive, infection by *C. difficile*, and at least two documented subsequent recurrences despite use of standard antibiotic therapy.
Kao D 2016 - abstract (FMT arm of RCT)	Double blind RCT (capsule vs fresh)	43 patients, mean 67 years, F:30/43 (70%). Two centres. 22 capsule group and 21 in colonoscopy group	Not reported

Kassam 2012	Case series	27 patients: the mean age was 69.4 years (range, 26-87 years) with 14 male subjects (52%) and 22 in-patients (81%).	Inclusion criteria were (1) laboratory-confirmed *C difficile* toxin using enzyme immunoassay with no other cause for diarrhea; (2) refractory CDI (defined as ongoing diarrhea despite antimicrobial treatment) or recurrent CDI (defined as symptom resolution for at least 2 days after discontinuation of treatment with recurrence of diarrhea);
Kelly 2012	Case series	26 recruited over 28 months;single centre;at least 3 recurrences of CDI following multiple antibiotic courses;adequate clinical and lab documentation post transplant; Mean age 59 (19-86 yrs); F: 24/26 (92%)	Method of CDI diagnosis not stated;mean duration of diagnosis of CDI prior to FMT 12.6 M (range 4 to 84 M);
Kelly 2014	Case series	retrospective study of immunocompromised patients receiving FMT for CDI; 80 patients data analysed from 16 centres;eligibilty assessed by 32 point questionairre;75 adults and 5 children; Mean age in Adults 53 (range 20-88) in children 10.9 (range 6.5-16); Adults (n=75) F:38 (48%)	4 categories; 1 recurrent/relapsing at least 3 episodes with failure of up to 8 week taper with vancomycin or at least 2 episodes of severeCDI resulting in hospitalisation and associated with significant morbidity.2 Refractory CDI-moderate CDI not responding to standard therapy for at least a week 3 Severe CDI elevated WBC., low albumin and abdominal tenderness. 4 complicated CDI- Admission to ITU, low blood pressure, fever, ileus, mental state changes, elevated WBC, high lactate and evidence of end organ failure

Kelly 2016	Double blind RCT (donor vs autologous FMT)	46 patients . Two centres. Donor FMT group n=22, mean age=48 (SD 16); F=18 (82%); Autologous FMT group n=24, mean age = 55(SD 14), F=19 (79%).	≥3 unformed stools over 24 hours for 2 consecutive days and either a positive stool test result for *C difficile* or pseudomembranes on colonoscopy
Khan 2014	Case series	retrospective analysis of 20 cases over 13 months (July 2012 to Aug 2013); selection criteria: all patients recieving FMT for CDI at their centre; single centre; adequate post transplant documentation and assessment; Demographic data presented seperately for community aquired and hospital aquired CDI; Calculated Overall Mean age 66.4 years; F 13 (65%); Mean number of CDI episodes pre-FMT:5.6 community aquired and 4.6 for hospital aquired	Method of CDI diagnosis not stated; data presented seperately for community aquired CDI and hospital aquired CDI; median duration of symptoms pre FMT for community aquired CDI was 7 months; 5 months for hospital aquired CDI
Kronman 2015	Case series	retrospective study of 10 children in single centre over 3 years (between Aug 2011 and May 2014); At least 3 episodes of CDI; adequate post transplant documentation and assessment; Mean age 5.4 years; F 7/10 (70%);	C diff toxin A&B and/or PCR; median duration of symptoms pre-FMT 250 days (range 90-541 days);
Lee 2014	Case series	retropsective analysis of 94 patients from 2008-2012; single centre; mixture of recurrent and refractory CDI definitions given; Mean age 71.8 years (range 24-95 years); F 53/94 (56.4%)	C diff toxin A&B and/or PCR; duration of symptoms pre-FMT not stated

Lee CH 2016 (FMT arm of RCT)	FMT arm of double blind RCT (Fresh vs Frozen)	219 patients, mean 73 years, F:146/219 (67%)	Toxin and PCR
MacConnachie 2009	Case series	retrospective analysis of 15 patients since 2003;single centre; recurrent CDI following succesful antibiotic therapy; Median age 81.5years (range 68-95); F 14/15 (93.3%)	Method of CDI diagnosis not stated;mean duration of diagnosis of CDI prior to FMT not stated
Mattila 2012	Case series	70 patients over 3 years (2007-2010) all laboratory confirmed recurrent CDI refractory to standard treatment. Mean age 73(22-90) F=42(60%). 60(86%) outpatients	positive culture and toxin; strain typing . Time from diagnosis to CDI mean 133 days (46-360). 36(51%0 had ribotype 027
Patel 2013	Case series	31 patients over 2 years (2011-2013) all had recurrent (at least 2 previouslt documented CDI episodes). Mean age 61 (SD19) F=17(55%).17/31 (55%) gi comorbdiity. Diverticulitis (5), IBS (5), UC (3), CD(2), gastroparesis (1), coloanal fistula(1)	Diagnosis method not stated. Medain time(range) from index diagnosis to FMT 340 days(18-2205)
Pathak 2014	Case series	12 patients with recurrent or relapsing CDI with at least 3 episodes and failure of treatment with vancomycin +/- additional antibiotic such as fidox or patients wuth at least two episodes of severe CDI or patients with moderate CDI not responding to vanc for a week or patients with severe/fulminant CDI not responding to standar treatment for 48 h. 12 patients over 3 years. mean age 72 (SD 15) range 37-90; F 8/12 (67%)	Diagnosis method not stated
Ray 2014	Case series	20 (August 2012-November 2013) 2 recurrences as defined by diarrhoea OR positive Cdiff after antibiotics (m,v,or f). Or if life threatening and/or admission to ICU. 20 patients mean age 62 (SD 18). F 16(80%). 15 (75%) out patients. Average time from diagnosis to FMT 49.6 weeks	Diagnosis method not stated

Rohlke 2010	Case series	19 patients over 5 years(September 2004-July 2009). At lesat 3 courses or treatment included vanc amn tapered vanc over 6 months.Mean age 49 (SD 15). F17 (90%). All out-patients	Diagnosis method confirmed by lab in all cases but method not specified
Rubin TA 2013	Case series, retrospective	74 patients (75 courses), mean age 63 years, F 49/74 (65%)	Diagnosis of CDI confirmed by lab only in a few cases. Method not specified.
Satokari R 2015	Case series, retrospective	49 patients, mean age 56 years, F 34/49 (69)	Culture and toxin
Tauxe 2016	Case series, retrospective	31 patients, mean age 77 years, F 18/31 (58%)	Not reported
Yoon 2010	Case series, retrospective	12 patients, mean age 66 years, F 9/12 (75%)	Toxin positivity or clinical findings
Youngster2014	Case series, prospective	20 patients, Median age 64.5; F 9/20 (45%). Exclusion criteria - delayed gastric emptying synd, recurrant aspiration, pregnancy, significant immunocompromise, history of signif food allergy to food included in donor diet.	Toxin and ELISA, PCR if toxin negative but ELISA is positive or indeterminate
Zainah 2015	Case series, retrospective	14 patients, mean age 73 years,	C. difficile toxin EIA and/or PCR

Brandt LJ 2012	Case series, retrospective	77 patients in 5 centres, mean age 65, F 56/77 (73%).	Not reported
Allegretti 2014	Case series, retrospective	22 patients, mean age 55, F 18/22 (82%)	C. difficile toxin EIA and/or PCR
Costello 2015	Case series, prospective	20 patients , median age 69 years, gender distribution not reported	Not reported
Agrawal 2016	multicentre, retrospective, lon term follow up study	146 patients, 100 (68.5%) women; mean age (range) 79.	Not reported
Dutta 2014	Case series, prospective	27 patients, mean age 64.5y, F 22/27 (81.5%)	Cdiff toxin positivity by ELISA
Emmanuelson 2014	Case series, retrospective	23 patients, mean age 66y, F 61%	Culture and/or toxin EIA

Van Nood 2013	FMT arm of RCT (FMT versus vancomycin)	From January 2008 through April 2010, 43 patients were randomly assigned to receive donor-feces infusion (17 patients), vancomycin (13), or vancomycin and bowel lavage (13). One patient assigned to receive donor-feces infusion was subsequently excluded from further analysis. Baseline demographics per groups: Donor Feces Infusion: 16 patients; mean age +/-SD (73 +/-13); F: 8/16 (50%); Vancomycin only: 13 patients; mean age +/-SD (66 +/-14); F: 7/13 (54%); Vancomycin and Bowel Lavage: 13 patients; mean age +/-SD (69 +/-16); F: 3/13 (23%)	Toxin and PCR. In 39 patients, a positive toxin test before inclusion was confirmed by a positive *C.difficile* culture. PCR ribotyping was performed on strains obtained from 34 patients
Youngster 2014	FMT arm of open-label RCT (NG versus colonic delivery of FMT)	37 patients were assessed for eligibility and 20 patients underwent randomisation: Colonoscopy arm: 10 patients, mean age +/-SD (50.4 +/- 28.8); F:6/10 (60%); Nasogastric tube:10 patients; mean age +/-SD (58.6 +/- 19.6); F: 5/10 (50%)	Toxin: initial toxin/glutamate dehydrogenase (GDH) enzyme-linked immunosorbent assay, followed by PCR only if the GDH test is positive or indeterminate, and does not routinely test for the NAP-1/B1/207 strain
Vigvari 2014	Case series, retrospective	30 patients, mean age 70.1 years (26-88 years), Female: 18/30 (60%)	Not reported

Patient characteristics			Donor Ch
Pre FMT Abx +/- other therapy (M,V,Fidox,IVG)/How many courses i.e M(2), V(1), IVG(1), Fidox(1). Were abx stopped prior to FMT	**Refractory / Recurrent**	**Flexi sigi / Colonoscopy findings**	**Healthy volunteer/Spouse/Related i.e mother/Other non related i.e friend**
Mean 3.6 courses of abs (range 2-7) abs varied (Clm, Cm, Cpfx, Ctri, Ctox, Amp, Gm, Clex, Mtz, Pen, Pip, tMp-SMZ, Taz, Lev, Tet, Vm) number of courses prior to transplant varied: 2-7; Recipients were pre-treated with vm (250mg q8h) for 4 or more days and this was discontinued the night before transplant.	recurrent (two or more lab confirmed relapses)	Not reported	15/18 were family members of recipient; no member availabe for remaining 3 so donors were healthy clinic staff. Hierachy of ideal donor described: intimate physical contact with patients (spouse/partner) > family houshold member > other healthy donor
Not stated	Not stated	Not reported	Healthy donors from OpenBiome stool bank mean age 36 years
All patients had antibiotics prior to diagnosis of CDI but specifics not stated; FMt group patients had 3 days vanc prior to FMT which stopped the day before; vanc group had 10 days of standard vanc followed by at least three weeks of pulsed vanc	recurrent with lab confirmation	6 out of 20 patients in FMT group had pseudomembranous colitis	Healthy volunteers less than 50 years old from which 16/20 donors related; 2 intimates; 2 unrelated
Not reported	split into refractory, recurrent and severe complicated	Colonoscopies done on most	Mix of healthy volunteers (319 69%) and family (143 31%)

Not reported	Recurrent	N/A	The donor is usually a family member of the patient who meets certain criteria, such as not having used antibiotics in the previous six months, being immunocompromised, and having no history of illicit drug use, tumors or inflammatory bowel disease.
The patients were treated with metronidazole or vancomycin until reduction of symptoms. All anti-microbial therapy was discontinued on the evening prior to stool transplantation.	Recurrent	1 patient with pseudomembranous colitis	Close relatives or other household members were selected as stool donors. Individuals without symptoms of gastrointestinal disease or a history of chronic infectious disease were considered suitable for stool donation.
At least one failed antibiotic regimen had to include a minimum of a 6-week course of tapered or pulsed vancomycin dosage, or at least a 1-month vancomycin course followed by a minimum of 2-week rifaximin "chaser."	Recurrent	Not reported	patients were asked to self-identify potential donors. These included mothers (n=2), daughters (n = 1), sons (n = 3), wives (n = 1), husbands (n = 1), and friends (n = 2).
Not reported	Recurrent	Not reported	Unrelated volunteers

All had at least metronidazole; 19 had subsequent vancomycin monotherapy. 8 had combination metronidazoleand vancomycin therapy.	Recurrent or refractory	Not reported	Two healthy volunteers served as donors and were evaluated for transmissible pathogens. The donors took no antibiotics for 6 months prior to stool donation.
antibiotics prior to CDI diagnosis- clind, cipro, metro, moxiflox, levoflox, azithro, cefurox, amox, augmentin; treatment for CDI-all had metronidazole, Sacchromyces bourladii, 4 had lactobacillus, 2 had IV IG, 19 had had rifaximin; pre-FMT all had 2 weeks of metronidazole or vanc, discontinued 2-3 days before FMT	recurrent at least 3 episodes (lab confirmation not stated)	11 had diverticular disease; 3 had colitis; 8 normal; 2 polyps; 2 haemorrhoids; 2 previous surgery	25/26 family memebers; 1 friend
79/80 had been treated with vancomycin. 55/80 had metronidazole, 23 had fidaxomicin, 13 had rifaximin and 30 had probiotics	recurrent CDI (at least 3 episodes and failure of vanc taper for 6-8 weeks); refractory (no improvement after 1 week of vanc); Severe CDI or complicated (definitions given)	Not reported	Not reported

3 or more recurrences of CDI and received a full course of vancomycin for their most recent acute episode.	Recurrent	Colonoscopies done on all	All prospective donors underwent a medical interview and physical examination and were excluded if they had a known communicable disease, features of the metabolic syndrome, a diarrheal disorder, an autoimmune or atopic disease, a tumor, a neurologic disorder, or chronic pain syndrome or if they had used antibiotics for any indication within 3 months. Potential donors also completed a modified AABB full-length donor history questionnaire, and those with risk factors for infectious agents were ex- cluded (Supplement).
Antibiotic treatment for CDI: metronidazole (1 patient had 1 course; 7 patients had 2 courses; 12 patients had 3 courses); vancomycin (2 patients had 1 course; 12 patients had 2 courses; 4 patients had 3 courses; 2 patients had pulsed vanc); 9 had fidaxomicin; all antibiotics stopped 48 hours before FMT	not explicityly stated but patients had a mean of 4.6-5.6 episodes of CDI prior to FMT	Not reported	5/20 from spouse/partner; 14/20 family member;1 non-relative
Antibiotics used prior to CDI diagnosis-metronidazole, augmentin, ampicillic, amoxycillin, cefdinir, cefuroxime, penicillin; CDI tretament all had metronidazole, 6/10 had vancomycin, 8/10 had vancomycin taper; pre-transplant all had vanc or fidaxomicin for 7 days, last dose given 24 hours pre-transplant	recurrent CDI; mean of 3.2 episodes pre-FMT	Not reported	9/10 parents; 1 sibling
Mean of 2,1 courses of antibiotics for CDI prior to FMT (metronidazole 79.3%, vancomycin 75%, vancomycin taper 15.2%, combination metro and vanc 17.4%, 3 patients had IVIG); pre-tranplant all antibiotic therapy for Cdi was discontinued 24 hours before FMT	recurrent (recurrent diarrhoea after at least 2 days of resolution following antibiotic therapy) or refractory (ongoing diarrhoea despite at least 5 days of oral vancomycin)	Not reported	2 unrelated donors

Metronidazole and Vancomycin	Both	Not reported	Unrelated volunteers
Antibiotics prior to CDI diagnosis not stated; 15/15 received metronidazole;15/15 received vanc, 3 received iVIG; vanc given pre-procedure but length of course not stated; stopped 12 hours before FMT	recurrent CDI defined as recurrence of diarrhoea after successful antibiotic therapy typically within 7 days of stopping antibiotics;	Not reported	related donors specifics not given
mean 4.5 courses of antibiotics. Metro, vanc, rifax, 1 IVIGStopped 36 hours before FMT	recurrent (two or more lab confirmed relapses)	Not reported	61(87%) family members; 9(13%) healthy donors
Stopped (usually vanc) 4 hours before bowel prep. Loperamide 4mg either before or immediately after FMT	recurrent (two or more lab confirmed relapses)	Not reported	"Mostly" family. 14 spouses, 9 children, 5 siblings, 3 parents, 1 niece, 1 friend
Antibiotics stopped 24 hours prior to procedure	Refractory / Recurrent and severe	8 colitis, 1 Cdiff, 1 haemorrhoid, 1 pseudomembranous colitis, 1 diverticulosis	10 family, 2 spouses
Antibiotics stopped 48 hours prior to procedure	16 recurrent; 4 severe/complicated	Not reported	10 family, 8 spouses, 2 healthy donors

Antibiotics stopped 1-3 days before FMT	recurrent	Not reported	4 family, 14 partner, 1 housemate
Vancomycin and / or metronidazole	Recurrent	Not reported	Healthy household members
Not reported	Refractory	Not reported	Frozen stool: 2 unrelated donors. Fresh stool: Family members, healthy volunteers, or the same universal donors.
Combinations of Vancomycin, Metronidazole, Fidoxamicin, Rifaximin	Both	Not reported	7 were from family members, rest were volunteers
Combination of metronidazole, vancomycin, rifaximin, bacitracin, nitazoxanide	Both	9/12 normal colonic mucosa, 3/12 had pseudomembranes	All family members (partner:8; child or grandchild:4)
Failed vancomycin taper and or fidaxomycin.	Refractory or recurrent. Defined 3 episodes of mild to moderate CDI or failure of 6-8 week taper with vancomycin, or atleast two episodes of severe CDI resulting in hospitalisation and associated with significant morbidity. Active CDI defined as more than 3 loose stools per day with a positive stool test.	Not reported	Unrelated adult volunteers
Vancomycin and / or metronidazole	Both	Not reported	12 from family members, 1 from unrelated volunteer

Failed on average of five conventional antimicrobial regimes; including metronidazole (81%), vancomycin (99% standard and pulsed) and/or tapered regime with or without rifaxmin (22%) or probiotics (77%).	Recurrent CDI (unresponsive to standard therapy)	Not reported	60% partners/spouses; 27% were either first degree relatives or otherwise related to the patient. ; one case - unknown person. In all, 56 of 77 donors resided in the same household as patient.
Several but eligibility included starting vancomycin for 7 days before procedure and stopping day before	Both. Relapsing defined as three or more episodes of CDI or refractory disease that is unreponsive to traditional antibiotics.	Not reported	Patient identified donors-spouse, family, friend. My co-inhabit
Not reported	Recurrent disease	Not reported	Healthy volunteers
Conventional therapy with met, van and/or fidaxomicin had failed in all. Some takinh probiotics. Om average	Recurrent defined as recurrentce of diarrhoea after completion of treatment. Severe CDI defined as low	Not reported	Donors usually identified by patient. One healthy volunteer not identified by patient
Most patients received metronidazole and/or vancomycin Other antibiotics included fidaxomicin, rifaximin.	Recurrent (>2 recurrences)	Active colitis seen in 26/27 patients with pseudomembranes in 2	Healthy donors selected via thorough clinical evaluation to exclude any transmissible disease. 10 spouse, 12 son or daughter, 1 parent, 4 friends.
Metronidazole and/or Vancomycin	Relapsing and recurrent	Not reported	Spouse or close relative of good health

At least one course of adequate antibiotic therapy (>=10 days of Vancomycin at a dose of >=125mg four times a day or >=10 days of Metronidazole at a dose of 500mg three times per day). In FMT group: patients received an abbreviated regimen of Vancomycin (500mg orally four times per day for 4 or 5 days), followed by bowel lavage with 4 liters of macrogol solution (Klean-Prep) on the last day of antibiotic treatment and the suspension of donor feces through a nasoduodenal tube the next day	Recurrent	Not done	Healthy volunteers <60 years of age (faces from 15 donors were used for 43 infusions in the infusion group and for patients who had a relapse after vancomycin treatment)
Patients had a median of 4 (range, 2-16) relapses prior to study enrollment, with 5 (range, 3-15) antibiotic treatment failures of a 6- to 8-week taper with Vancomycin (95% of patients) with or without an alternative antibiotic, including Fidaxomicin (70% of participants).Patients were required to discontinue all antibiotics at least 48 hours prior to the procedure	Relapsing or recurring (having at least 3 episodes of mild-to-moderate CDI OR at least 2 episodes of severe CDI resulting in hospitalization and associated with significant modbidity	Not reported	Healthy volunteer donor: nonpregnant adults, 18-50 years of age, on no medications, with a normal body mass index
Not clear from paper, but it appears most patients had vancomycin	Refractory and recurrent	Not reported	Donors were relatives in 22 cases (73.3%) and unrelated volunteers in 8 cases (26.7%).

aracteristics	FMT characteristics		
Screening and abx cessation	**Fresh/Frozen, Route administered**	**Sample preparation Transplant sample sourcing, screening, preparation; , volume, mixing solution, storage and time from collection to transplant**	**Proceedure: Bowel Prep/Drugs used prior to FMT i.e Moviprep 2 sachets/PPI (dose), prokinetic (dose), Loperamide FMT administration Follow up method**
Within 30 days before donation (usually 7 days) screened: Blood:HAV (HAV ab (IgM and IgG), HBV (ab to HepB surface antigen and core antigen), HCV (HCV ab RIBA-II), HIV-1 & 2 (EIA), Treponema pallidum (rapid plasma reagin test). Stool: C diff (Toxin A or B (cytotoxin) detection), enteric bacterial pathogens (selective stool culture), ova/parasites (light microscopy) No antimicrobial therapy in previous 6 months	Fresh nasogastric, with tube placement on morning of transplant and tube tip placement confirmed by radiography	Stool obtained 6 or less hours prior to transplant. Approx 30g or 2cm^3 preferably soft stool selected and homogenised in 50-70ml 0.9N sterile saline (household blender - slow speed setting initially, rising gradually to maximum and continued then for 2-4 min) until sample smooth. Filtered through coffee paper filter x2 allowing adequate time for slow filtration to end.	20mg omeprazole evening before and morning of transplant. 25ml of stool suspension adminitered then tube flushed with 25ml sterile 0.9N saline. Tube removal. Normal diet and physical activites allowed immediately. Follow up by telephone or clinic visit and stool specimens examined for c.diff toxin A in most patients.
open Biome Criteria followed	Frozen pills	Not stated	Not described
no antibiotics for 6 months; stool tested for C. diff , enteric pathogens, ova and parasites, MDR gram nehgatives, MRSA, VRE; Serum tested for Hep A, Hep B, Hep C, HIV 1 and 2, strongyloides, treponema, Entamoeba. High risk lifestyle, FH of GI cancer, IBD, systemic diseases, personal GI disease	fresh via colonoscopy	Mean time from donation to infusion was 3.8 hours;mass of donation not stated but mixed with 500mls saline and blended and strained; delivered to right colon through colonoscope	2 groups FMT group received 4L of macrogol bowel cleansing solution for 1-2 days on the last 2 days of vancomycin followed by FMT. The other group had bowel cleansing and vancomycin standard treatment.
Sporicidal disinfection was performed in patient rooms as per institutional protocols; specific instruc- tions with handouts regarding sporicidal home cleaning were provided to patients to prevent reinfection.	Fresh or frozen via Colonoscopy and NG tube	Not reported	Not reported

Some tests are performed for screening: serology for hepatitis A, B and C, human immunodeficiency virus (HIV), fecal parasitology, fecal test for Clostridium difficile, and fecal culture.	Fresh via enteroscope	Mixed in N. Saline. Volume and other variables not stated	Not reported
Donors were screened for hepatitis A, B and C and HIV infection, as well as enteric bacterial pathogens including Salmonella, Shigella, Campy-lobacter and Yersinia species.	Fresh via Gastroscopy or colonoscopy	A fresh stool sample of 50–100 g was obtained from the donor on the day of the instillation procedure. The stool sample was spread out onto a gauze pad which was then placed in a strainer. The gauze was flushed with 250 ml sterile 0.9% NaCl and the resulting suspension was collected and aspirated into syringes. A flexible videogastroscope was intro- duced into the distal duodenum. Approximately 200 ml of sample solution was introduced	No bowel prep given to colonic delivered FMT
The donorshad to submit their medical records and underwent serologic testing for HIV and Hepatitis B and C, and stool testing that included screening for routine enteric pathogens, *C. difficile* toxin B, and examination for ova and parasites, and *Giardia* and *Cryptosporidium* antigens. Donors were excluded if they had GI co-morbidities or had used antibiotics within 3 months.	Fresh or frozen via Colonoscopy	Approximately 50g of fecal material was placed into a standard commercial blender (Oster, Subeam, Rye, NY) and homogenized in 250 ml of sterile, non-bacteriostatic normal saline. Faceal suspension, if stored , was put in 10% glycerol and stored at -80 for up to 8 weeks. The frozen preparation was diluted in 250ml salne before infusion.	Patients were maintained on full dose of vancomycin (125mg, four times daily by mouth) until 2 days before the FMT proce- dure. The day before the procedure, the patients were prepped using a split dosage polyethylene glycol purge (GoLYTELY or MoviPrep), which is standard in our endoscopy unit, before colonoscopies to wash out residual antibiotic and fecal material.
Not reported	Oral capsules vs colonoscopy	Not reported	Not reported

Blood was screened for hepatitis B surface antigen, hepatitis C antibody, Helicobacter pylori and syphilis serologic markers, human immunodeficiency virus types 1 and 2, and human T-lymphotropic virus types I and II. Stool was processed for enteric bacterial pathogens, C difficile toxin, and ova and parasites.	Retention enema	Approximately 150 g of fresh stool collected was emulsified in 300 mL of sterile water. The supernatant component was administered rectally by en- ema.	All CDI therapy was discontinued at least 24 hours prior to FT.
no antibiotics in preceding 90 days; blood for HAV, HBV, HCV, HIV 1&2, Treponema pallidum; stool for culture for bacteria, stain for ova and parasites, C. diff. toxin A and B	Fresh via colonoscopy	stool obtained 6 hours or less prior to transplant6=8 tablespoons of donor stool added and shaken in 1litre of sterile water passed through gauze. Aliquoted in 60ml syringes.	polyethelene glycol bowel prep night before transplant; 500-960mls administered via scope mainly to rightcolon; Avoid defecating for 30-45 mins
Not reported	fresh or frozen not stated; 12 of 16 centres used colonoscopy route	Not reported	prep not stated; questionnaire sent out to 16 centres to retrospectively collect data; method of follow up at each centre not stated but had to have data for at least 12 weeks to be eligible for inclusion

Testing for HIV-1 and HIV-2 was performed within 2 weeks before donation for FMT. Other serologic and stool testing was performed within 1 month before FMT and included testing for hepatitis A, B, and C viruses; testing for Treponema pallidum; polymerase chain reaction (PCR) testing for detection of C difficile toxin; culture for enteric pathogens (Esch erichia coli, Salmonella, Shigella, Yersinia, Campylobac- ter, Listeria monocytogenes, Vibrio parahaemolyticus, and V cholerae); testing for fecal Giardia and Cryptosporidium antigens; acid-fast stain for detection of Cyclospora and Isospora; ova and parasite testing; and enzyme immunoassay for detection of Rotavirus.	Fresh via colonoscopy	The protocol specified a “dose” of 100 g of stool diluted in 500 mL of nonbacteriostatic 0.9% normal sa- line immediately before the procedure, but the study relied on fresh stool, which has unpredictable weight and volume, and most provided specimens were less than 100 g.	Donors took an osmotic laxative (magnesium hydroxide) the evening before and provided fresh stool the day of FMT. All donor specimens were transported on ice and processed within 6 hours of collection. Patients were given a standard bowel purge (sodium sul- fate, potassium sulfate, and magnesium sulfate oral solution) the evening before the procedure. For patient convenience, sodium sulfate, potassium sulfate, and magnesium sulfate oral solution was substituted for the polyethylene glycol (PEG) bowel purge described in the study protocol.
no antibiotics for 3 months; stool tested for C. diff toxin PCR, enteric pathogens, ova and parasites, Cryptosporidium, Microspora; Serum tested for Hep A, Hep B, Hep C, HIV 1 and 2; H. pylori' Human T lymphotropic virus	fresh via colonoscopy	stool obtained within 30 mins of transplantation; 50g of stool into 200mls of saline and blended; Aspirated into single 60ml syringe for delivery	4 litres polyethelene glycol bowel prep; 60mls administered via scope into right colon; follow up combination of clinic, telephone and questionairres
no antibiotics for 3 months; stool tested for C. diff , enteric pathogens, ova and parasites; Serum tested for Hep A, Hep B, Hep C, HIV 1 and 2; CMV, EBV, high risk behaviours, systemic antineoplastic drugs, immunosuppressives, history of GI disease. Directed donors to avoid foods which recipient may be allergic to for 5 days prior.	fresh via NGT	time from collection to transplant not stated; 30g stool added to 100mls saline and blended;filtered throgh gauze; 30-60mls infused	8.5g-17g polyethylene glycol in 8oz of water 3 times a day for 2 days prior to FMT; omeprazole 1mg/kg orally day before and on day of FMT; follow up all patients called 2 days after FMT, further follow up combination of clinic, telephone and repeat C. diff. testing
no antibiotics for 6 months; stool tested for C. diff , enteric pathogens, ova and parasites, norovirus,enterovirus; Serum tested for Hep A, Hep B, Hep C, HIV 1 and 2, human lT-cell ymphotrophic virus 1&2, treponema	retention enema	time from collection to transplant not stated; 150g stool added to 300mls water and homogenised with spatula 100mls infused	no bowel prep stated;100mls infused via enema;follow up methods not stated but retrospective analysis extracted from clinical record

Questionnaire. Pathogens, HIV, HABC, CMV, EBV, syphilis, strongyloides, entamoeba. Screening every 4 months	Fresh and Frozen. Lower GI route	100g of stool homogensied and mixed in 300mls of water. If frozen kept for 30 days at -20C. If fresh administered within 24hrs.	Nil
Within 30 days before donation (usually 7 days) screened: Blood:HAV (HAV ab (IgM and IgG), HBV (ab to HepB surface antigen and core antigen), HCV (HCV ab RIBA-II), HIV-1 & 2 (EIA), Treponema pallidum (rapid plasma reagin test). Stool: C diff (Toxin A or B (cytotoxin) detection), enteric bacterial pathogens (selective stool culture), ova/parasites (light microscopy) No antimicrobial therapy in	Fresh via NGT	time between stool collection and transplant not stated; 30g of stool blended with 150mls saline and filtered; 30mls infused via NGT	no bowel prep stated;30mls infused via NGT;omeprazole given prior to FMT; follow up methods not stated but retrospective analysis extracted from clinical record
No antibiotics for 6 months. Blood for FBC, CRP, protein,creatinine, LFTs, HBV, HCV, HIV 1 &2, treponema. Stools for Cdiff, pathogens, OCP,	Fresh, within 6 hours colonoscopic	Stool obtained 6 or less hours prior to transplant. Homogenised in 100-200ml water.	Colonic lavage ith 4l PE solution.
No antibiotics for 3 months. Excluded chronic gastrointestinal condirions, active peptic ulcer disease, GERD, IBS,IBD,polyps, mlaignancy. Blood for HABCV, HIV, Treponema, stool for culture, OCP, cryptosporidium, microsporidia, Cdiff	Fresh, colonoscope	Donors given 30ml MgOh evening before donation. Stools within 6 hours of passage blended with 100ml Nsaline and sieved for delivery.	Bowel prep for colonoscopy (not stated which), 4mg operamide either before or after FMT
High risk behaviours, no antibiotics for 3 months, Blood for HIV, HABC, STDs, stooll for bacterial culture, OCP, Cdiff	Fresh, colonoscope (11); 1 nasoduodenal	Donor given mg citrate before. stool collected within 6 hours of preocedure. 6-8 tablespoons to 1l tap water, shaken.	PEG bowel prep, 400-500 ml to TI/Right colon. Patients given 2 tablets of diphenoxylate/atropine. A week later 2 month course of Saccharomyces boulardii
3 unscreened. High risk behaviours, antibiotics in 3 months, blood for HIV, HABC, terponema, stool for Cdiff, bacterial culture, OCP, Giardia, Cryptosporidium,	Fresh, colonoscope	Time between donation and colonoscopy not stated	On day of treatment patients given 2 imodium tablets 2 hours prior and 1 after. Bowel prep not recorded.

Selective based on discretion. Blood from some for viruses (HABC, HIV), stool from some for Cdiff and enteric pathogens	Fresh colonoscope	Time between donation and colonoscopy not stated	PEG bowel prep. Some (not clear how many) had 2 immodium immediately after and then again6 hours after FMT
Screened for occult infectious conditions and no abx use in preceeding 3 months	Fresh, Upper GI (NG or PEG)	30 g of donor stool in mixed in saline. 25mls given in an infusion.	Pre-treated with 3 days of vancomycin and proton pump inhibitor prior to procedure
No significant medical history, no antibiotics for prior six months. Donor feces were screened for enteric pathogens and blood was screened for antibodies to hepatitis A, B, and C; HIV; and Treponema pallidum within 2 weeks of donations	Fresh: 26 patients; Frozen: 23 patients. Administered by colonoscopy	30g of stool in 200mls of saline or glycerol. If frozen stored in -80C for up to 16 weeks.	Polyethylene glycol prior to procedure
Not reported	Fresh, both routes	Not reported	Not reported
Donor feces were screened for enteric pathogens and blood was screened for antibodies to hepatitis A, B, and C; HIV	Fresh via colonoscopy	Stool collected morning of transplant, filtered and mixed with saline. 250 - 400mls infused into patient.	Abx stopped 3 days prior to FMT
Age range 18-50 years, BMI 18.5 - 25. No significant medical history, not pregnant, no antibiotics for prior six months. Donor feces were screened for enteric pathogens and blood was screened for antibodies to hepatitis A, B, and C; HIV; and Treponema pallidum within 2 weeks of donations. Donors refrain from common allergens for 5 days before donation.	Capsule (oral) frozen for mean of 113 days (range 30-252 days).	Each inoculum was prepared from the feces of a single donor. The final slurry was concentrated by centrifugation and resuspended in saline at one-tenth the volume. Fecal matter solution was pipetted into size 0 capsules (650 μL), which were closed and then secondarily sealed in size 00 capsules. Capsules were stored frozen at −80°C (−112°F) till use. A full treatment of 30 capsules contained sieved, concentrated material derived from a mean of 48 g of fecal matter (mean per capsule, 1.6 g; range, 1.0-2.05 g). Samples stored for 4 weeks without use to allow for retesting for HIV, hep B and C. (full screening and exclusion details given in appendix)	Abx stopped 48 hrs prior to FMT
Donor feces were screened for enteric pathogens and blood was screened for antibodies to hepatitis A, B, and C; HIV	Fresh. Upper GI in 13 patients, lower GI in 1 patient	Fresh stool sample (30–50 g) homogenized and mixed with water. About 120–180 ml of the suspension was instilled through NGT; 300–500 ml was administered if IMT was done via colonoscopy.	Abx stopped 24 hrs prior to FMT and given proton pump inhibitor prior to procedure

Excluded if abx within preceding 3 months. Exclusion criteria also included immunosuppressive agents, including chemotherapeutic agents; had known or recent exposure to HIV,hepatitis B or C;had a current communicable disease; participated in high-risk sexual behaviors; used illicit drugs; had a history of incarceration; traveled within 6 months to areas with endemic diarrheal illnesses; or had history of infl ammatory bowel disease, irritable bowel syndrome or chronic diarrhea, gastrointestinal malignancy or polyposis). Blood tested for HIV, Hep A/B/C and stool for OCP and giardia antigen and cryptosporidium	Fresh (within 8 hours), colonoscopy	Suspended in saline, mixed by hand or blender, filtered and infused as 300 to 700 mls	Abx stopped 48 to 72 hrs prior to FMT. Bowel prep given before procedure
no abs for 3 months. No laxatives, hstory of constipation, no history of GI disease, travel in 3 months, not on immunosuppressives or chemo. No metabolic syndrome, autoimmune, atopic disease	Fresh (within 6 hours), colonoscopy	Fresh in blender 500ml Nsaline, strained. 60ml drawn up in 8-9 syringes per patient.	Abs stopped prior to procedure.
screening as per FDA guidelines 2011	Frozen stool (> 2 months in 16 patients and <2 months in 4 patients), colonoscopy route in 19, jejunal	30g in 120ml N.saline, divided into 50ml aliquots	Not reported
Excluded if "history of antibiotic use" (time not specified), high risk behaviour, prisoners, GI disease,	Fresh. Initial FMT in 118(81%) colonoscope, 13(9%) OGD, 3(2%)	Milk of magnesia to donors. 60-100g stool suspended in 300-500ml nsaline, mixed, sieved. 75-200ml for upper route (OGD, enteroscopy), 250-400ml colnoscopically,	Bowel prep given. Loperamide after FMT
Blood and stool screened for transmissible diseases	Fresh, given via a combination of jejunal and colonic route	25-30g of stool given as 180mls via enteroscopy and 270mls via colonoscopy	Not mentioned
Potential donors were accepted only if serum antibodies against HIV 1 and 2, hepatitis C virus, and hepatitis B surface antigen were negative, as were stool cultures for Salmonella, Shigella, Campylobacter, enterohemolytic Escherichia coli, and Clostridium	Fresh, given as enema (lower GI	50g of fresh faeces prepared in an anaerobic cabinet by adding and stirring small portions of pre-reduced and pre-warmed (37 °C) sterile isotonic saline, to a total of 500 ml.	Not mentioned

Questionnaire adressing risk factors for potencially transmissible diseases. Donor feces were screened for parasites, including Blastocystis hominis and Dientamoeba fragilis; C.difficile, and enteropathogenic bacteria. Blood was screened for HIV; human T-cell lymphotropic virus types 1 and 2; hepatitis A,B, and C; cytomegalovirus; Epstein-Barr virus; Treponema pallidum; Strongyloides stercoralis; and Entamoeba histolytica. A dnor pool was created, and screening was repeated every 4 months. Before donation, another questionaire was used to screen for recent illnesses.	Fresh via nasoduodenal tube	Feces were collected by the donor on the day of infusion and immediately transported to the hospital. Feces were diluted with 500mls of sterile saline 0.9%. This solution was stirred, and the supernatant strained and poured in a sterile bottle. A mean (+-SD) of 141+-71g of feces was infused. The mean time from defecation to infusion was 3.1+-1.9 hours	Bowel lavage with 4 liters of macrogol solution (Klean-Prep) on the last day of antibiotic treatment. Within 6 hours after collection of feces by the donor, the solution was infused through a nasoduodenal tube (2 to 3 minutes per 50mls). The tube was removed 30 minutes after the infusion, and patients were monitored for 2 hours. Patients kept a stool diary and were questioned about stool frequency and consistency, medication use, and adverse effects. Stool tests for C.difficile toxin were performed on days 14,21,35, and 70 and whenever diarrhoea occured.
Volunteers were excluded for any significant past medical history or any use of antibiotics in the preceeding 6 months. Initial screening using the American Association of Blood Banks donor questionaire for exposure to infectious agents. Physical examination and general laboratory screening tests (within 30 days of donations). All results had to be within normal range for age and sex. Donor feces were screened for enteric bacterial	Frozen via colonoscopy or NGT	Donors were asked to take a dose of milk of magnesia the day before fecal collections to facilitate manipulation of the sample. A fecal suspension was generated in normal saline without preservatives, using commercial blender. Materials were passed through 4 sieves to remove particulate material. The final slurry was concentrated 3-fold by centrifugation and then resuspended in sterile saline with 10% glycerol added as a bacterial cryoprotectant. Inocula were then frozen at -80 C pending use. Each sieved inoculum was calculated to have been derived from approximately 41g of fecal material. Inocula were stored frozen for up to 156 days, range, 29-156 days; frozen material was thawed in a 37 C water bath, and then kept on ice until delivery.	Subjects assigned to colonoscopic administration underwent a standard bowel preparation with 4 liters of PEG solution, followed by endoscopic administration to the right colon of 90 cc thawed inoculum:further diluted to 250cc for adults and 160 cc for paediatric patients. Patients were given a single oral dose of loperamide at the time of procedure. Subjects assigned to NGT delivery of FMT were
Pre-medical examination was carried out with a questionnaire in order to rule out high-risk individuals (such as drug use, promiscuity, known illness, taking antibiotics or trips abroad in the past six months). Stool samples	Fresh stool delivered via nasogastric route in 15 patients and nasoduodenal route in 15 patients	60 grams, it was placed in 200 mL of mortar physiological saline (0.9%) and harvested. then the homogenate of 4 × 4 cm was filtered sterile gauze pads transferred to another vessel and finally were taken from the filtrate up to 100 ml syringe and given to patient within 6 hours.	Antibiotics were stopped prior to transplant and patients were given laxatives. Patients received both metoclopramide and high dose proton pump inhibitor on the day of the transplant.

Total no of infusions	Define primary outcome	Outcome 1 infusion	1 or more infusions	Total follow up period
not explicitly stated. Data implies a single infusion on a single occasion for each patient	Not explictly stated, but authors report outcome based on symptom resolution and / or CDI toxin negativity	15/16 (94%)	15/16(94%)	90 days post transplantion, assessed by examination of medical records.
NA	Clinical resolution of diarrhoea at 8 weeks	NA	19/20 (95%)	Not reported
13/20 had 1 FMT; 6/20 had co-existent PMC and received infusions every 3 days until symptom resolution (4 had 2 infusions, 1 had 3 infusions and 1 had 4 infusions	Resolution of diarrhoea 10 weeks after the end of the treatments	13/20(65%)	18/20(90%)	primary end point 10 weeks after end of treatment
Not reported	Early Failure rate defined as non-response or recurrence of diarrhoea with either toxin or PCR positive CDI within 1 month of FMT	not reported	375/462 (81.2%)	3 months

1 infusion via enteroscopy	not defined in paper but implied symptom free to end of follow up	10/12 (83%)	10/12 (83%)	6 months
I infusion via gastroscopy or colonoscopy	successful treatment defined as no further contact with the clinic due to CDI symptoms within 80 days of FMT	29/40 (73%)	33/40 (82.5%)	80 days
4 of 43 had repeat infusion	Not specified	37/43 (86%)	41/43 (95%)	12 months
1 infusion via colonoscopy or 1 course of capsules.	Defined as cure but no time period given	41/43 (95%)	41/43 (95%)	Not specified

Five patients underwent a second FT because of ongoing diarrhea; 3 had symptom resolution and 2 continued to experience diarrhea despite 2 FTs.	resolution of symptoms- no time period defined	22/27 (81%)	25/27 (93%)	mean follow-up at 427.3 days after transplant.
not explicitly stated but imples single infusion for all patients	Prevention of further CDI relapse and/or significant diarrhoea requiring vancomycin; time frame for outcome not stated	24/26 (92.3%)	24/26 (92.3%)	follow up mean 10.7 months ranged from 2-30 months
78 patients had single infusion; 12 patients had 2 infusions	response defined as absence of diarrhoea or marked reduction in stool frequency and without need for further antibiotics within 12 weeks after 1 or more FMTs	62/80 (77.5%)	70/80 (87.5%)	minimum of 12 weeks required; mean follow up 11m (range 3-46m)

1 infusion via colonoscopy	Resolution of diarrhoea without need for anti CDI therapy during 8 week follow up	20 / 22 (90.9%)	21 / 22 (90.9%)	8 weeks for efficacy, 6 months for safety
18 had single infusion; 2 had 2 infusions	Resolution of diarrhoea without recurrence of symptoms within 3 months of FMT	18/20 (90%)	20/20 (100%)	minimum of 6 months (range not stated)
9 patients had single infusion, 1 patient had 2 infusions	Not defined in paper but implied symptom free to end of follow up	9/10 (90%)	10/10 (100%)	median duration of follow up 44 days (range 13-700 days)
if no resolution of diarrhoea after 7 days post FMT then further enema give. Range given 1-10(46/94 had 1 FMT, 20/94 had 2 FMT, 17/94 had 3 FMT, 11/94 had 4 or more)	Cured following FMT if no recurrence of diarrhoea at 6 months follow up	45/94 (47.9%)	81/94 (86.2%)	6-24 months

1, if no response at day 4, then further FMT and if no response then FMT or abx. Primary outcome based on up to 2 FMTs.	Clinical resolution of diarrhea without relapse at 13 weeks	113/219 (52%)	193/219 (88.1%)	13 weeks
14/15 had 1 FMT;1/15 had 2 FMT	Not explicitly stated but implied that "cure" was no symptoms at follow up after 1 FMT	11/15 (73%)	12/15(80%)	median 16 weeks (4 weeks to 24 weeks) not predefined
67 had 1; 3 had 2	Resolution diarrhea without a positive C difficile toxin stool test at 12 weeks	63/70 (90%)	66/70 (94%)	1 year. 4 with initial favourable response had replase after receiving antibiotics. 2 of these were successfully treated with FMT; 2 with recurrent antibitics for CDI
28 had 1; 3 had 2	Not defined.	26/30 (87%)	29/30 (97%)	1 year 6 out of 6 maintained imrpovemement
1 infusion in all but 1 patient who had repeat via ND route	No strict definition. Authors state : 'A successful treatment was determined by the resolution of diarrhea, a fall in white cell count, or absence of fever and an improvement in vital signs'.	11/12 (92%)	12/12 (100%)	No recurrences within 90 days of FMT. Total follow up from 2 to 29 months
1	Resolution defined as positive stools after FMT.	20/20 (100%)	20/20 (100%)	Follow up mean 3 months (range 0-10)

1	not defined in paper but implied symptom free to end of follow up	19/20 (95%)	20/20 (100%)	6 months to 5 years
1	Resolution of diarrhea without recurrence within 60 days of FMT	59/75 (79%)	59/75 (79%)	60 days
1	Resolution of diarrhoea with a negative C. difficile toxin stool test at 3 months	47/49 (96%)	47/49 (96%)	All followed up for 12 weeks and 42 patients followed up for 1 year
1 infusion in 27 patients, multiple infusions in 4 patients	Resolution was defined as the absence of significant diarrhea (diarrhea as defined by at least three episodes per day) or a marked reduction in diarrhea not requiring antibiotic therapy.	24/31 (77%)	27/31 (87%)	Mean 9 months (range 2–24)
1	Clinical response was defined as absence of diarrhea, cramps, and fever within 3 to 5 days of transplant	12/12 (100%)	12/12 (100%)	3 weeks to 8 years
N/A	Response defined as less than 3 bowel movements in 24 hrs	NA	18/20 (90%)	Primary outcome based on 8 weeks however patients followed up for 6 months
1 in 10 patients, 2 in 2 patients, and 3 in 2 patients received three FMTs	Defined as less than 3 loose bowel movements a day for 2 consecutive days after FMT and no need for further CDI therapy on day 7.	8/14 (57%)	11/14 (79%)	100 days

1 infusion in 75 patients, 2 infusions in 2 patients	Resolution without recurrence within 90 days including those that needed a second infusion or antibiotics	70/77 (91%)	70/77 (91%)	Minimum 90 days, but median 17 months
1 infusion	Primary outcome not defined	19/22 (86%)	21/22 (95%)	Range 2 weeks to 17 months with ave length 3 months
1 infusion in 17 patients, 2 infusions in 3 patients	Resolution of diarrhoea and/or absence of CDI toxin in stool as measured by PCR after at least 3 months follow up	17/20 (85%)	20/20 (100%)	Minimum 3 months (but up to 14 months)
146 had one infusion, 12 out of 25 early recurrences had another	Initial Resolution of CDI symptoms with no recurrence after 12	121/146 (82.9%)	121/146 (82.9%)	mean follow up 12.3 (range 1-48) months
1	Resolution of diarrhoea and disappearance of stool Cdiff toxin	27/27 (100%)	27/27 (100%)	Ranged from 9.7 -34 months (mean 20.6 months)
1 in 22 patients and 2 in 1 patient	Resolution of diarrhoea in 3 days with no recurrence in 3 months	15/23 (65%)	16/23 (70%)	Median follow up of 18 months (range 0-201 months)

16 patients had 1 infusion; 3 who did not respond in this group had 2nd infusion.	Cure without relapse within 10 weeks after the initiation of therapy. For patients in the infusion group who required a second infusion of donor feces, follow up was extended to 10 weeks after the second infusion. Cure was defined as an absence of diarrhoea or persisent diarrhoea that could be explained by other causes with three consecutive negative stool tests for C.difficile toxin. Relapse was defined as diarrhoea with a positive stool test for C.difficile toxin.	13/16 (81%)	15/16(94%)	After first infusion at 10 weeks; follow up was extended to 10 weeks after the second infusion
20 patients in both study arms had one infusion (14 was cured after the first infusion (70%)). One patient in the NGT arm refused subsequent retreatment. The ramaining 5 patients were given a second infusion (4 patients obtained cure after second infusion, resulting in an overall cure rate of 90%).	Clinical resolution of diarrhoea off antibiotics for C.difficile, without relapse within 8 weeks. For patients who required a second treatment dose, a follow-up was calculated starting at the time of the second administration.	14/20 (70%)	18/20 (90%)	8 weeks follow up for primary response
1 infusion in 27 patients and 2 infusions in 3 patients.	Primary cure rate was defined as resolution of symptoms without recurrence within 6 weeks after a single FMT, while secondary cure rate was calculated	27/30 (90%)	29/30 (97%)	6 weeks

Adverse events - mild	Adverse events - serious
no mention	2 patients died between transplant and follow up stool testing for c.diff toxin. One had end stage renal disease and was receiving peritoneal dialysis. Developed peritonitis 3 days post transplant and died shortly after. The second patieint died 14 days post transplant of pneumonia complicating COPD and atherosclerosis (study authors state: *"the possibility that the use of the nasogastric tube contributed to the peritonitis cannot be excluded"*)
None reported	none reported
none in vanc group; FMT group 19/20 had transient diarrhoea, 12/20 had abdominal pain and bloating	2 deaths in FMT arm
Not reported	Not reported formally

Not reported	None
Not reported	5 deaths; The remaining 5 patients had serious co-morbid conditions and died 3 weeks–2 months after the FDIT procedure. Two of these 5 patients were seriously weakened after long lasting diarrhoeal disease, 1 being the oldest patient in the series (94 y). Additionally, 1 patient had advanced stage Wegener's granulomatosis with complications, 1 patient had acute myelogenous leukaemia requiring repeated antibiotic treatment for other infections, and 1 patient with advanced cardiovascular disease developed fulminant colitis and underwent subtotal colectomy, and subsequently died of complications.
Not reported	Not reported
Transient nausea and vomiting	None

Not reported	Not reported
mild diarrhoea post FMT in 3 patients	no serious adverse events
self limited diarrhoea in 3, fever in 1, bloating and abdo discomfort in 3, hip pain in 1, Crohn's flare in 1, Pertussis in 1, nausea in 1, minor mucosal tear at colonoscopy in 1	deaths- 1 due to pneumonia, 1 due to aspiration at time of colonoscopy; hospitilisations- 1 due to fever and encephalopathy, 1 due to abdo pain after FMT, 3 due to IBD flare, 1 colectomy, 1 hip fracture, 1 influenza, catheter infection

Chills were reported more frequently after autologous than donor FMT (P = 0.053). Rates of other solicited AEs (fever, abdominal pain, bloating, nausea, vomiting, diarrhea, flatulence, anorexia, and constipation) did not differ significantly between groups.	There were no SAEs related to FMT.
self limited diarrhoea in 4; abdominal pain in 3; nausea in 2; fatigue 13	none stated
vomiting post FMT in 1; mucoid stools for 2 days after FMT	none stated
10% had transient constipation and flatulence post FMT	6 deaths due to critical illness, not felt to be due to FMT or CDI directly but these 6 are included in the 8 who failed to respond overall

Transient diarrhoea (70%), abdominal cramps (10%), nausea (5%) in 24 hours post FMT; constipation (20%) and flatulence (25%) in follow up period	19 deaths in total 13 week study period (unrelated). 12 patients required hospitalization because of ilnesses unrelated to FMT
none	none stated
None reported	None related to FMT
Not reported	Micro-perforation but not related to FMT. One death at 3 months afer due to ,metastatic pancreatic cancer.
None reported	None related to FMT
1 pain/nausea after colonoscopy, 1 continued diarrhoea (CDIFF neg) ? Bile salt malabsorption after cholecystectom, 2 transient bloat/ cramps	1 perforation related to colonoscopy sealed with clip

None reported	none reported
None	None
Mild transient fever in 2 (frozen FMT)	3 deaths (unrelated)
Worsening arthritis, constipation, diarrhoea, urinary tract infection.	5 deaths; not attributed to FMT. Stroke, myocardial infarction, aspiration pnuemonia, hospitalisation for CDI not as a consequnce of FMT.
Not reported	None
Transient abdominal cramping and bloating in 6 patients (30%) that resolved in 72 hours	1 hospitalised with a documented relapse of severe CDI after taking 15 capsules but had successful treatment after receiving the remaining 15 capsules after discharge. No other severe adverse events (grade 2 or above).
Not reported	4 deaths within 30 days of FMT unrelated to FMT.

None reported	4 patients reported a new medical condition after FMT (peripheral neuropathy, Sjogrens, ITP and rheumatoid arthritis
pain in one patient	none
None	None
CDI-negative diarrhoea in 7(4.8%) and constipation in 4(2.7%)	within 12 weeks-6 hospitalizations due to CDI and/or FMT. One debilitated
Low grade fever (18.5%) and bloating (11.1%)	None
Nil	Nil

94% immediate diarrhoea, 31% abdominal pain with cramping, 19% belching - resolved within 3 hours. During follow up 3 patients had constipation (19%). 2 patient had infections: one patient with recurrent UTI had UTI	1 hospitalisation for symptomatic choledocholithiasis (unrelated)
Mild abdominal discomfort and bloating in 4 patients (20%). One child treated colonoscopically had a transient fever of 38.8 C on day 2 that resolved spontaneously	2 deaths (unrelated), 1 new diagnosis of malignancy (unrelated), 1 hospitalisation for Fournier gangrene (unrelated)
Nausea in one patient. Nil else	Nil

Study characteristics			
Name et al Year	**RCT characteristics**	**Arms of RCT**	**No. of patients, mean or median age, Gender distribution**
Lee CH 2016	**Double blind RCT comparing fresh vs frozen FMT**	Overall	219 patients, mean 73 years, F:146/219 (67%)
		Frozen	108 patients, mean 73 years, F:72/108 (67%)
		Fresh	111 patients, mean 73 years, F:74/111 (67%)
Kao D 2016 (abstract)	**RCT comparring capsule versus colonoscopy delivered FMT**	Overall	43 patients, mean 67 years, F:30/43 (70%)
		Capsule	22 patients, mean 66 years, F:17/22 (77%)
		Fresh (colonoscopy)	21 patients, mean 68 years, F:13/21 (62%)
Cammarota 2015	**RCT comparing FMT versus vancomycin**	FMT	20 patients , mean 71 years, F:12/20 (60%)
		Vancomycin	19 patients , mean 79 years, F:11/19 (60%)
Allegretti 2016 (abstract)	**RCT comparing FMT versus vancomycin**	high dose capsules FMT	9 patients demographics not stated (abstract)
		low dose capsules FMT	10 patients demographics not stated (abstract)
Kelly 2016	**Double blind RCT comparing donor vs placebo (autologous) FMT**	donor FMT	22 patients, mean 48 years, F:18/22 (82%)
		autologous FMT	24 patients, mean 55 years, F:19/24 (78%)
Van Nood 2013	**RCT comparing FMT versus vancomycin**	Vancomycin abbreviated regime (500mg orally four times per day for 4 or 5 days) with bowel lavage and FMT	16 patients; mean age +/-SD (73 +/-13); F: 8/16 (50%)
		Vancomycin standard regime (500mg orally four times per day for 14 days)	13 patients; mean age +/-SD (66 +/-14); F: 7/13 (54%)
		Vancomycin standard regime(500mg orally four times per day for 14 days) with bowel lavage on day 4 or 5.	13 patients; mean age +/-SD (69 +/-16); F: 3/13 (23%)
Youngster 2014	**RCT comparing NG versus colonic**	Frozen (colonoscopy)	10 patients, mean age +/-SD (50.4 +/-28.8); F:6/10 (60%)

Youngster 2014	versus colonic delivery of FMT	Frozen (NGT)	10 patients; mean age +/-SD (58.6 +/-19.6); F: 5/10 (50%)

Patient characteristics		
Diagnosis of C.diff i.e Elisa/PCR, duration from diagnosis to transplant	**Pre FMT Abx +/- other therapy (M,V,Fidox,IVG)/How many courses i.e M(2), V(1), IVG(1), Fidox(1). Were abx stopped prior to FMT**	**Refractory / Recurrent**
Toxin and PCR	Metronidazole and Vancomycin	Both
Not reported	Not reported	Recurrent
CDI diagnosis confirmed by toxin; in 23/39(59%) positive culture as well as toxin.mean duration of CDI diagnosis prior to FMT not stated	All patients had antibiotics prior to diagnosis of CDI but specifics not stated; FMt group patients had 3 days vanc prior to FMT which stopped the	Recurrent with lab confirmation
Not stated	Not stated	Not stated
≥3 unformed stools over 24 hours for 2 consecutive days and either a positive stool test result for C difficile or pseudomembranes on colonoscopy	3 or more recurrences of CDI and received a full course of vancomycin for their most recent acute episode.	Recurrent
Toxin and PCR	At least one course of adequate antibiotic therapy (>=10 days of Vancomycin at a dose of >=125mg four times a day or >=10 days of Metronidazole at a dose of 500mg three times per day). In FMT group: patients received an abbreviated regimen of Vancomycin (500mg orally four times per day for 4 or 5 days), followed by bowel lavage with 4 liters of macrogol solution (Klean-Prep) on the last day of antibiotic treatment and the suspension of donor feces through a nasoduodenal tube the next day.	Recurrent
Toxin: initial toxin/glutamate dehydrogenase (GDH) enzyme-linked immunosorbent assay, followed by	Patients had a median of 4 (range, 2-16) relapses prior to study enrollment, with 5 (range, 3-15) antibiotic	Relapsing or recurring (having at least 3 episodes of mild-to-moderate CDI OR at least 2 episodes of severe CDI

PCR only if the GDH test is positive or indeterminate, and does not routinely test for the NAP-1/B1/207 strain.	treatment failures of a 6- to 8-week taper with Vancomycin with or without an alternative antibiotic.	at least 2 episodes of severe CDI resulting in hospitalization and associated with significant modbidity.

	Donor char
Flexi sigi / Colonoscopy findings	**Healthy volunteer/Spouse/Related i.e mother/Other non related i.e friend**
Not done	Unrelated volunteers
Not reported	Unrelated volunteers
6 out of 20 patients in FMT group had pseudomembranous colitis	16/20 donors related; 2 intimates; 2 unrelated
Not reported	Healthy donors from OpenBiome stool bank mean age 36 years
Colonoscopies done on all	All prospective donors underwent a medical interview and physical examination and were excluded if they had a known communicable disease, features of the metabolic syndrome, a diarrheal disorder, an autoimmune or atopic disease, a tumor, a neurologic disorder, or chronic pain syndrome or if they had used antibiotics for any indication within 3 months. Potential donors also completed a modified AABB full-length donor history questionnaire,
Not done	Healthy volunteers <60 years of age (faces from 15 donors were used for 43 infusions in the infusion group and for patients who had a relapse after vancomycin treatment).
Colonoscopy or NGT	Healthy volunteer donor: nonpregnant adults, 18-50 years of age, on no medications, with a normal body mass

colonoscopy or NGT	of age, on no medications, with a normal body mass index.

racteristics		
Screening and abx cessation	**Fresh/Frozen, Route administered**	**Sample preparation Transplant sample sourcing, screening, preparation; , volume, mixing solution, storage and time from collection to transplant**
Questionnaire. Pathogens, HIV, HABC, CMV, EBV, syphilis, strongyloides, entamoeba. Screening every 4 months	Fresh vs Frozen. Lower GI route	100g of stool homogensied and mixed in 300mls of water. If frozen kept for 30 days at -20C. If fresh administered within 24hrs.
Not reported	Oral capsules vs colonoscopy	Not reported
No antibiotics for 6 months; stool tested for C. diff , enteric pathogens, ova and parasites, MDR gram nehgatives, MRSA, VRE; Serum tested for Hep A, Hep B, Hep C, HIV 1 and 2, strongyloides, treponema,	FMT delivered fresh via colonoscopy	mean time from donation to infusion was 3.8 hours;mass of donation not stated but mixed with 500mls saline and blended and strained; deliverd to
open Biome Criteria followed	Frozen pills	Not stated
Testing for HIV-1 and HIV-2 was performed within 2 weeks before donation for FMT. Other serologic and stool testing was performed within 1 month before FMT and included testing for hepatitis A, B, and C viruses; testing for Treponema, PCR detection of C difficile toxin; culture for enteric pathogens (Escherichia coli, Salmonella, Shigella, Yersinia, Campylobacter, Listeria, Vibrio, and V cholerae); testing for Giardia and Cryptosporidium, ova and parasite	Fresh via colonoscopy	The protocol specified a “dose” of 100 g of stool diluted in 500 mL of nonbacteriostatic 0.9% normal sa- line immediately before the procedure, but the study relied on fresh stool, which has unpredictable weight and volume, and most provided specimens were less than 100 g.
Questionnaire adressing risk factors for potencially transmissible diseases. Donor feces were screened for parasites, including *Blastocystis hominis* and *Dientamoeba fragilis*; C.difficile, and enteropathogenic bacteria. Blood was screened for HIV; human T-cell lymphotropic virus types 1 and 2; hepatitis A,B, and C; cytomegalovirus; Epstein-Barr virus; *Treponema pallidum*; *Strongyloides stercoralis*; and *Entamoeba histolytica*. A dnor pool was created, and screening was repeated every 4 months. Before donation, another questionaire was used to screen for recent illnesses.	Fresh via nasoduodenal tube	Feces were collected by the donor on the day of infusion and immediately transported to the hospital. Feces were diluted with 500mls of sterile saline 0.9%. This solution was stirred, and the supernatant strained and poured in a sterile bottle. A mean (+-SD) of 141+-71g of feces was infused. The mean time from defecation to infusion was 3.1+-1.9 hours.
Volunteers were excluded for any significant past medical history or any use of antibiotics in the preceeding 6 months. Initial screening using the American Association of Blood Banks donor questionaire for exposure to infectious agents. Physical examination and general	Frozen via colonoscopy or NGT	Donors were asked to take a dose of milk of magnesia the day before fecal collections to facilitate manipulation of the sample. A fecal suspension was generated in normal saline without

infectious agents. Physical examination and general laboratory screening tests (within 30 days of donations). All results had to be within normal range for age and sex. Donor feces were screened for enteric bacterial pathogens including rotavirus, *Listeria monocytogenes*, *Vibrio*	frozen via colonoscopy or NGT	generated in normal saline without preservatives, using commercial blender. Materials were passed through 4 sieves to remove particulate material. The final slurry was

FMT Characteristics		
Proceedure: Bowel Prep/Drugs used prior to FMT i.e Moviprep 2 sachets/PPI (dose), prokinetic (dose), Loperamide FMT administration Follow up method	**Total no of infusions**	**Define primary outcome**
Nil	1, if no response at day 4, then further FMT and if no response then FMT or abx. Primary outcome based on up to 2 FMTs.	Clinical resolution of diarrhea without relapse at 13 weeks
Not reported	1 infusion via colonoscopy or 1 course of capsules.	Defined as cure but no time period given
FMT group received 4L of macrogol bowel cleansing solution for 1-2 days prior to procedure; patients followed up propectively by referring physicians;	13/20 had 1 FMT; 6/20 had co-existent PMC and received infusions every 3 days until symptom resolution (4 had 2 infusions, 1 had 3 infusions and 1 had 4	Resolution of diarrhoea 10 weeks after the end of the treatments
Not described	NA	Clinical resolution of diarrhoea at 8 weeks
Donors took an osmotic laxative (magnesium hydroxide) the evening before and provided fresh stool the day of FMT. All donor specimens were transported on ice and processed within 6 hours of collection. Patients were given a standard bowel purgethe evening before the procedure.	1 infusion via colonoscopy	Resolution of diarrhoea without need for anti CDI therapy during 8 week follow up
Bowel lavage with 4 liters of macrogol solution (Klean-Prep) on the last day of antibiotic treatment. Within 6 hours after collection of feces by the donor, the solution was infused through a nasoduodenal tube (2 to 3 minutes per 50mls). The tube was removed 30 minutes after the infusion, and patients were monitored for 2 hours. Patients kept a stool diary and were questioned about stool frequency and consistency, medication use, and adverse effects. Stool tests for C.difficile toxin were performed on days 14,21,35, and 70 and whenever diarrhoea occured.	16 patients had 1 infusion; 3 who did not respond in this group had 2nd infusion	Cure without relapse within 10 weeks after the initiation of therapy. For patients in the infusion group who required a second infusion of donor feces, follow up was extended to 10 weeks after the second infusion. Cure was defined as an absence of diarrhoea or persisent diarrhoea that could be explained by other causes with three consecutive negative stool tests for C.difficile toxin. Relapse was defined as diarrhoea with a positive stool test for C.difficile toxin.
Subjects assigned to colonoscopic administration underwent a standard bowel preparation with 4 liters of PEG solution, followed by endoscopic administration to the right colon of 90	20 patients in both study arms had one infusion (14 was cured after the first infusion (70%)). One patient in the NGT arm refused subsequent retreatment.	Clinical resolution of diarrhoea off antibiotics for C.difficile, without relapse within 8 weeks. For patients who required a second treatment

administration to the right colon of 90 cc thawed inoculum:further diluted to 250cc for adults and 160 cc for paediatric patients. Patients were given a single oral dose of loperamide	The ramaining 5 patients were given a second infusion (4 patients obtained cure after second infusion, resulting in an overall cure rate of 90%).	who required a second treatment dose, a follow-up was calculated starting at the time of the second administration.

Results		
Primary outcome	**One infusion**	**One or more infusion**
Intention to treat: 159/219 (73%) at 13 weeks	113/219 (52%)	193/219 (88.1%)
Intention to treat: 81/108 (75%) at 13 weeks	57/108 (52.8%)	98/109 (90.7%)
Intention to treat: 78/111 (70%) at 13 weeks	56/111 (50.5%)	95/111 (85.6%)
41/43 (95%)	Not reported	41/43 (95%)
20/22 (91%)	Not reported	20/22 (91%)
21/21 (100%)	Not reported	21/21 (100%)
18/20 (90%)	13/20 (65%)	18/20 (90%)
5/19 (26%)	Not applicable	Not applicable
7/9 (77% resolution of diarrhoea at 8 weeks)	Not applicable	Not applicable
7/10 (70%) resolution of diarrhoea at 8 weeks	Not applicable	Not applicable
In the intention-to-treat analysis, 20 of 22 patients (90.9%) in the donor FMT group achieved clinical cure at 8 weeks	22/20 (90.9%)	22/20 (90.9%)
com- pared with 15 of 24 (62.5%) in the autologous FMT group (P = 0.042)	15/24 (62.5%)	15/24 (62.5%)
13/16 (81%) after first infusion at 10 weeks; overall 15/16 (94%) after second infusion, follow up was extended to 10 weeks after the second infusion	13/16 (81%)	15/16(94%)
4/13 (31%) patients at 10 weeks	15/24 (62.5%)	15/24 (62.5%)
3/13 (23%) patients at 10 weeks	15/24 (62.5%)	15/24 (62.5%)
8 out of 10 (80%) at **8 weeks primary response**; overall cure rate 100% after 2nd infusion but via NGT	8/10 (80%)	10/10 (100%)

6 out of 10 (60%) at **8 weeks primary response**; overall cure rate 80% after second infusion via NGT	6/10 (60%)	8/10 (80%)

Adverse events - serious
19 deaths in total 13 week study period (unrelated).
6 deaths (unrelated to FMT)
13 deaths (unrelated to FMT)
None
None
None
2 deaths (unrelated to FMT)
none
Not stated (abstract)
Not stated (abstract)
None
None
1 hospitalisation for symptomatic choledocholithiasis (unrelated).
1 death (unrelated)
None
2 deaths (unrelated), 1 new diagnosis of malignancy (unrelated)

1 hospitalisation for Fournier gangrene (unrelated)

Study details			
Name et al Year	**Type of study i.e RCT, case control etc**	**No. of patients, years, location, selection criteria, Mean or median age, Gender distribution; other**	**Diagnosis of C.diff i.e Elisa/PCR, duration from diagnosis to transplant**
Aas 2003	Case series	19 recruited over 9 years (1994-2002) at a single centre (USA); two or more lab confirmed relapses after initial specific AB treatment, adequate clin and lab documentation of post transplant course; Mean age 73±9 (SEM) (Range: 51-88 years); F: 13/18 (72%); Hospitalised=5; nursing home=3; outpatient-GI clinic=10)	Lab confirmed via stool sample, toxin A only, then B added from 2001. 2 or more positive test stool tests (mean 3.2, range 2-7). Mean period from diagnosis of c/diff colitis and stool transplantation 102±24 (SEM) days (range 25-497)
Allegretti 2016	Open label cluster dose finding trial comparing low dose (30 pills) vs high dose (30 pills on 2 consecutive days)	19-age/gender not stated	Diagnosis method not stated
Cammarota 2015	Open label RCT	prospective RCT comparing FMT plus vancomycin to vancomycin therapy alone for recurrent CDI; 39 patients over 12 months July 2013 to June 2014; single centre; FMT group (n=20) mean age 71 years (range 29-89) F 12 (60%); Vanc group (n=19) mean age 75 (49-93) F 11 (58%)	CDI diagnosis was based on symptoms and toxin confirmed in 23/39(59%) positive ulture.mean duration of CDI diagnosis prior to FMT not stated

Fischer et al. 2016	Retrospective cohort study	Of 328 patients in the developmental cohort, 73.5% (N=241) were females with a mean age of 61.4±19.3 years; 19.2% (N=63) had inflammatory bowel disease (IBD), and 23.5% (N=77) were immunocompromised. Two academic centres. 2011-2015. Of 134 patients in the validation cohort, 57% (N=77) were females with a mean age of 66±18.1 years; 9.7% (N=13) had IBD, and 17.9% (N=24) were immunocompromised. Single centre. 2011-2015	Diagnosis of Cdiff if recurrent at least 3 episodes of CDI and failure of 6-8 week vancomycin taper. Severe based on albumin, elevated white cell count and abdominal pain. Severe complicated defined as admission to ITU hypotension, fever, ileus, reduced GCS, elevated white cell count and lactate with end organ dysfunction.
Ganc et al 2015	Case series, retrospective	12 patients. No other variables reported	Not reported
Garborg et al. 2010	Case series, retrospective	39 patients (one had 2 FMTs). Treated single centre 1994-2008. Mean age 75y (range 53-94). F=21 (53%)	Toxin positivity or clinical findings (37/40 toxin positive)

Hamilton et al. 2012	Case series	43 patients. Single centre. 29 non-IBD and 14 IBD patients. Non IBD cohort (mean age 64.7y SEM 3.3; F 20 (69%)); IBD cohort (mean age 44.6 SEM 5.8; F 11 (79%))	Inclusion criteria for FMT included a history of symptomatic, toxin-positive, infection by *C. difficile*, and at least two documented subsequent recurrences despite use of standard antibiotic therapy.
Kao D 2016 - abstract (FMT arm of RCT)	Double blind RCT (capsule vs fresh)	43 patients, mean 67 years, F:30/43 (70%). Two centres. 22 capsule group and 21 in colonoscopy group	Not reported
Kassam et al. 2012	Case series	27 patients: the mean age was 69.4 years (range, 26-87 years) with 14 male subjects (52%) and 22 in-patients (81%).	Inclusion criteria were (1) laboratory-confirmed *C difficile* toxin using enzyme immunoassay with no other cause for diarrhea; (2) refractory CDI (defined as ongoing diarrhea despite antimicrobial treatment) or recurrent CDI (defined as symptom resolution for at least 2 days after discontinuation of treatment with recurrence of diarrhea);
Kelly 2012	Case series	26 recruited over 28 months;single centre;at least 3 recurrences of CDI following multiple antibiotic courses;adequate clinical and lab documentation post transplant; Mean age 59 (19-86 yrs); F: 24/26 (92%)	Method of CDI diagnosis not stated;mean duration of diagnosis of CDI prior to FMT 12.6 M (range 4 to 84 M);

Kelly 2014	Case series	retrospective study of immunocompromised patients receiving FMT for CDI; 80 patients data analysed from 16 centres;eligibilty assessed by 32 point questionairre;75 adults and 5 children; Mean age in Adults 53 (range 20-88) in children 10.9 (range 6.5-16); Adults (n=75) F:38 (48%)	4 categories; 1 recurrent/relapsing at least 3 episodes with failure of up to 8 week taper with vancomycin or at least 2 episodes of severeCDI resulting in hospitalisation and associated with significant morbidity.2 Refractory CDI-moderate CDI not responding to standard therapy for at least a week 3 Severe CDI elevated WBC., low albumin and abdominal tenderness. 4 complicated CDI- Admission to ITU, low blood pressure, fever, ileus, mental state changes, elevated WBC, high lactate and evidence of end organ failure
Kelly et al. 2016	Double blind RCT (donor vs autologous FMT)	46 patients . Two centres. Donor FMT group n=22, mean age=48 (SD 16); F=18 (82%); Autologous FMT group n=24, mean age = 55(SD 14), F=19 (79%).	≥3 unformed stools over 24 hours for 2 consecutive days and either a positive stool test result for *C difficile* or pseudomembranes on colonoscopy

Khan 2014	Case series	retrospective analysis of 20 cases over 13 months (July 2012 to Aug 2013); selection criteria: all patients recieving FMT for CDI at their centre; single centre; adequate post transplant documentation and assessment; Demographic data presented seperately for community aquired and hospital aquired CDI; Calculated Overall Mean age 66.4 years; F 13 (65%); Mean number of CDI episodes pre-FMT:5.6 community aquired and 4.6 for hospital aquired	Method of CDI diagnosis not stated; data presented seperately for community aquired CDI and hospital aquired CDI; median duration of symptoms pre FMT for community aquired CDI was 7 months; 5 months for hospital aquired CDI
Kronman 2015	Case series	retrospective study of 10 children in single centre over 3 years (between Aug 2011 and May 2014); At least 3 episodes of CDI; adequate post transplant documentation and assessment; Mean age 5.4 years; F 7/10 (70%);	C diff toxin A&B and/or PCR; median duration of symptoms pre-FMT 250 days (range 90-541 days);
Lee 2014	Case series	retropsective analysis of 94 patients from 2008-2012; single centre; mixture of recurrent and refractory CDI definitions given; Mean age 71.8 years (range 24-95 years); F 53/94 (56.4%)	C diff toxin A&B and/or PCR; duration of symptoms pre-FMT not stated
Lee CH 2016 (FMT arm of RCT)	FMT arm of double blind RCT (Fresh vs Frozen)	219 patients, mean 73 years, F:146/219 (67%)	Toxin and PCR

MacConnachie 2009	Case series	retrospective analysis of 15 patients since 2003;single centre; recurrent CDI following succesful antibiotic therapy; Median age 81.5years (range 68-95); F 14/15 (93.3%)	Method of CDI diagnosis not stated;mean duration of diagnosis of CDI prior to FMT not stated
Mattila 2012	Case series	70 patients over 3 years (2007-2010) all laboratory confirmed recurrent CDI refractory to standard treatment. Mean age 73(22-90) F=42(60%). 60(86%) outpatients	positive culture and toxin; strain typing . Time from diagnosis to CDI mean 133 days (46-360). 36(51%0 had ribotype 027
Patel 2013	Case series	31 patients over 2 years (2011-2013) all had recurrent (at least 2 previouslt documented CDI episodes). Mean age 61 (SD19) F=17(55%).17/31 (55%) gi comorbdiity. Diverticulitis (5), IBS (5), UC (3), CD(2), gastroparesis (1), coloanal fistula(1)	Diagnosis method not stated. Medain time(range) from index diagnosis to FMT 340 days(18-2205)
Pathak 2014	Case series	12 patients with recurrent or relapsing CDI with at least 3 episodes and failure of treatment with vancomycin +/- additional antibiotic such as fidox or patients wuth at least two episodes of severe CDI or patients with moderate CDI not responding to vanc for a week or patients with severe/fulminant CDI not responding to standar treatment for 48 h. 12 patients over 3 years. mean age 72 (SD 15) range 37-90; F 8/12 (67%)	Diagnosis method not stated

Ray 2014	Case series	20 (August 2012-November 2013) 2 recurrences as defined by diarrhoea OR positive Cdiff after antibiotics (m,v,or f). Or if life threatening and/or admission to ICU. 20 patients mean age 62 (SD 18). F 16(80%). 15 (75%) out patients. Average time from diagnosis to FMT 49.6 weeks	Diagnosis method not stated
Rohlke 2010	Case series	19 patients over 5 years(September 2004-July 2009). At lesat 3 courses or treatment included vanc amn tapered vanc over 6 months.Mean age 49 (SD 15). F17 (90%). All out-patients	Diagnosis method confirmed by lab in all cases but method not specified
Rubin TA 2013	Case series, retrospective	74 patients (75 courses), mean age 63 years, F 49/74 (65%)	Diagnosis of CDI confirmed by lab only in a few cases. Method not specified.
Satokari R 2015	Case series, retrospective	49 patients, mean age 56 years, F 34/49 (69)	Culture and toxin
Tauxe 2016	Case series, retrospective	31 patients, mean age 77 years, F 18/31 (58%)	Not reported
Yoon 2010	Case series, retrospective	12 patients, mean age 66 years, F 9/12 (75%)	Toxin positivity or clinical findings

Youngster2014	Case series, prospective	20 patients, Median age 64.5; F 9/20 (45%). Exclusion criteria - delayed gastric emptying synd, recurrant aspiration, pregnancy, significant immunocompromise, history of signif food allergy to food included in donor diet.	Toxin and ELISA, PCR if toxin negative but ELISA is positive or indeterminate
Zainah 2015	Case series, retrospective	14 patients, mean age 73 years,	C. difficile toxin EIA and/or PCR
Brandt LJ 2012	Case series, retrospective	77 patients in 5 centres, mean age 65, F 56/77 (73%).	Not reported
Allegretti	Case series, retrospective	22 patients, mean age 55, F 18/22 (82%)	C. difficile toxin EIA and/or PCR
Costello	Case series, prospective	20 patients , median age 69 years, gender distribution not reported	Not reported

Agrawal 2016	multicentre, retrospective, lon term follow up study	146 patients, 100 (68.5%) women; mean age (range) 79.	Not reported
Dutta 2014	Case series, prospective	27 patients, mean age 64.5y, F 22/27 (81.5%)	Cdiff toxin positivity by ELISA
Emmanuelson 2014	Case series, retrospective	23 patients, mean age 66y, F 61%	Culture and/or toxin EIA
Van Nood 2013	FMT arm of RCT (FMT versus vancomycin)	From January 2008 through April 2010, 43 patients were randomly assigned to receive donor-feces infusion (17 patients), vancomycin (13), or vancomycin and bowel lavage (13). One patient assigned to receive donor-feces infusion was subsequently excluded from further analysis. Baseline demographics per groups: Donor Feces Infusion: 16 patients; mean age +/-SD (73 +/-13); F: 8/16 (50%); Vancomycin only: 13 patients; mean age +/-SD (66 +/-14); F: 7/13 (54%); Vancomycin and Bowel Lavage: 13 patients; mean age +/-SD (69 +/-16); F: 3/13 (23%)	Toxin and PCR. In 39 patients, a positive toxin test before inclusion was confirmed by a positive *C.difficile* culture. PCR ribotyping was performed on strains obtained from 34 patients
Youngster 2014	FMT arm of open-label RCT (NG versus colonic delivery of FMT)	37 patients were assessed for eligibility and 20 patients underwent randomisation: Colonoscopy arm: 10 patients, mean age +/-SD (50.4 +/-28.8); F:6/10 (60%); Nasogastric tube:10 patients; mean age +/-SD (58.6 +/- 19.6); F: 5/10 (50%)	Toxin: initial toxin/glutamate dehydrogenase (GDH) enzyme-linked immunosorbent assay, followed by PCR only if the GDH test is positive or indeterminate, and does not routinely test for the NAP-1/B1/207 strain
Vigvari 2014	Case series, retrospective	30 patients, mean age 70.1 years (26-88 years), Female: 18/30 (60%)	Not reported

Patient characteristics			Donor Ch
Pre FMT Abx +/- other therapy (M,V,Fidox,IVG)/How many courses i.e M(2), V(1), IVG(1), Fidox(1). Were abx stopped prior to FMT	**Refractory / Recurrent**	**Flexi sigi / Colonoscopy findings**	**Healthy volunteer/Spouse/Related i.e mother/Other non related i.e friend**
Mean 3.6 courses of abs (range 2-7) abs varied (Clm, Cm, Cpfx, Ctri, Ctox, Amp, Gm, Clex, Mtz, Pen, Pip, tMp-SMZ, Taz, Lev, Tet, Vm) number of courses prior to transplant varied: 2-7; Recipients were pre-treated with vm (250mg q8h) for 4 or more days and this was discontinued the night before transplant.	recurrent (two or more lab confirmed relapses)	Not reported	15/18 were family members of recipient; no member availabe for remaining 3 so donors were healthy clinic staff. Hierachy of ideal donor described: intimate physical contact with patients (spouse/partner) > family houshold member > other healthy donor
Not stated	Not stated	Not reported	Healthy donors from OpenBiome stool bank mean age 36 years
All patients had antibiotics prior to diagnosis of CDI but specifics not stated; FMt group patients had 3 days vanc prior to FMT which stopped the day before; vanc group had 10 days of standard vanc followed by at least three weeks of pulsed vanc	recurrent with lab confirmation	6 out of 20 patients in FMT group had pseudomembranous colitis	Healthy volunteers less than 50 years old from which 16/20 donors related; 2 intimates; 2 unrelated

Not reported	split into refractory, recurrent and severe complicated	Colonoscopies done on most	Mix of healthy volunteers (319 69%) and family (143 31%)
Not reported	Recurrent	N/A	The donor is usually a family member of the patient who meets certain criteria, such as not having used antibiotics in the previous six months, being immunocompromised, and having no history of illicit drug use, tumors or inflammatory bowel disease.
The patients were treated with metronidazole or vancomycin until reduction of symptoms. All anti-microbial therapy was discontinued on the evening prior to stool transplantation.	Recurrent	1 patient with pseudomembranous colitis	Close relatives or other household members were selected as stool donors. Individuals without symptoms of gastrointestinal disease or a history of chronic infectious disease were considered suitable for stool donation.

At least one failed antibiotic regimen had to include a minimum of a 6-week course of tapered or pulsed vancomycin dosage, or at least a 1-month vancomycin course followed by a minimum of 2-week rifaximin "chaser."	Recurrent	Not reported	patients were asked to self-identify potential donors. These included mothers (n=2), daughters (n = 1), sons (n = 3), wives (n = 1), husbands (n = 1), and friends (n = 2).
Not reported	Recurrent	Not reported	Unrelated volunteers
All had at least metronidazole; 19 had subsequent vancomycin monotherapy. 8 had combination metronidazoleand vancomycin therapy.	Recurrent or refractory	Not reported	Two healthy volunteers served as donors and were evaluated for transmissible pathogens. The donors took no antibiotics for 6 months prior to stool donation.
antibiotics prior to CDI diagnosis- clind, cipro, metro, moxiflox, levoflox, azithro, cefurox, amox, augmentin; treatment for CDI-all had metronidazole, Sacchromyces bourladii, 4 had lactobacillus, 2 had IV IG, 19 had had rifaximin; pre-FMT all had 2 weeks of metronidazole or vanc, discontinued 2-3 days before FMT	recurrent at least 3 episodes (lab confirmation not stated)	11 had diverticular disease; 3 had colitis; 8 normal; 2 polyps; 2 haemorrhoids; 2 previous surgery	25/26 family memebers; 1 friend

79/80 had been treated with vancomycin. 55/80 had metronidazole, 23 had fidaxomicin, 13 had rifaximin and 30 had probiotics	recurrent CDI (at least 3 episodes and failure of vanc taper for 6-8 weeks); refractory (no improvement after 1 week of vanc); Severe CDI or complicated (definitions given)	Not reported	Not reported
3 or more recurrences of CDI and received a full course of vancomycin for their most recent acute episode.	Recurrent	Colonoscopies done on all	All prospective donors underwent a medical interview and physical examination and were excluded if they had a known communicable disease, features of the metabolic syndrome, a diarrheal disorder, an autoimmune or atopic disease, a tumor, a neurologic disorder, or chronic pain syndrome or if they had used antibiotics for any indication within 3 months. Potential donors also completed a modified AABB full-length donor history questionnaire, and those with risk factors for infectious agents were ex- cluded (Supplement).

Antibiotic treatment for CDI: metronidazole (1 patient had 1 course; 7 patients had 2 courses; 12 patients had 3 courses); vancomycin (2 patients had 1 course; 12 patients had 2 courses; 4 patients had 3 courses; 2 patients had pulsed vanc); 9 had fidaxomicin; all antibiotics stopped 48 hours before FMT	not explicityly stated but patients had a mean of 4.6-5.6 episodes of CDI prior to FMT	Not reported	5/20 from spouse/partner; 14/20 family member;1 non-relative
Antibiotics used prior to CDI diagnosis-metronidazole, augmentin, ampicillic, amoxycillin, cefdinir, cefuroxime, penicillin; CDI tretament all had metronidazole, 6/10 had vancomycin, 8/10 had vancomycin taper; pre-transplant all had vanc or fidaxomicin for 7 days, last dose given 24 hours pre-transplant	recurrent CDI; mean of 3.2 episodes pre-FMT	Not reported	9/10 parents; 1 sibling
Mean of 2,1 courses of antibiotics for CDI prior to FMT (metronidazole 79.3%, vancomycin 75%, vancomycin taper 15.2%, combination metro and vanc 17.4%, 3 patients had IVIG); pre-tranplant all antibiotic therapy for Cdi was discontinued 24 hours before FMT	recurrent (recurrent diarrhoea after at least 2 days of resolution following antibiotic therapy) or refractory (ongoing diarrhoea despite at least 5 days of oral vancomycin)	Not reported	2 unrelated donors
Metronidazole and Vancomycin	Both	Not reported	Unrelated volunteers

Antibiotics prior to CDI diagnosis not stated; 15/15 received metronidazole;15/15 received vanc, 3 received iVIG; vanc given pre-procedure but length of course not stated; stopped 12 hours before FMT	recurrent CDI defined as recurrence of diarrhoea after successful antibiotic therapy typically within 7 days of stopping antibiotics;	Not reported	related donors specifics not given
mean 4.5 courses of antibiotics. Metro, vanc, rifax, 1 IVIGStopped 36 hours before FMT	recurrent (two or more lab confirmed relapses)	Not reported	61(87%) family members; 9(13%) healthy donors
Stopped (usually vanc) 4 hours before bowel prep. Loperamide 4mg either before or immediately after FMT	recurrent (two or more lab confirmed relapses)	Not reported	"Mostly" family. 14 spouses, 9 children, 5 siblings, 3 parents, 1 niece, 1 friend
Antibiotics stopped 24 hours prior to procedure	Refractory / Recurrent and severe	8 colitis, 1 Cdiff, 1 haemorrhoid, 1 pseudomembranous colitis, 1 diverticulosis	10 family, 2 spouses

Antibiotics stopped 48 hours prior to procedure	16 recurrent; 4 severe/complicated	Not reported	10 family, 8 spouses, 2 healthy donors
Antibiotics stopped 1-3 days before FMT	recurrent	Not reported	4 family, 14 partner, 1 housemate
Vancomycin and / or metronidazole	Recurrent	Not reported	Healthy household members
Not reported	Refractory	Not reported	Frozen stool: 2 unrelated donors. Fresh stool: Family members, healthy volunteers, or the same universal donors.
Combinations of Vancomycin, Metronidazole, Fidoxamicin, Rifaximin	Both	Not reported	7 were from family members, rest were volunteers
Combination of metronidazole, vancomycin, rifaximin, bacitracin, nitazoxanide	Both	9/12 normal colonic mucosa, 3/12 had pseudomembranes	All family members (partner:8; child or grandchild:4)

Failed vancomycin taper and or fidaxomycin.	Refractory or recurrent. Defined 3 episodes of mild to moderate CDI or failure of 6-8 week taper with vancomycin, or atleast two episodes of severe CDI resulting in hospitalisation and associated with significant morbidity. Active CDI defined as more than 3 loose stools per day with a positive stool test.	Not reported	Unrelated adult volunteers
Vancomycin and / or metronidazole	Both	Not reported	12 from family members, 1 from unrelated volunteer
Failed on average of five conventional antimicrobial regimes; including metronidazole (81%), vancomycin (99% standard and pulsed) and/or tapered regime with or without rifaxmin (22%) or probiotics (77%).	Recurrent CDI (unresponsive to standard therapy)	Not reported	60% partners/spouses; 27% were either first degree relatives or otherwise related to the patient. ; one case - unknown person. In all, 56 of 77 donors resided in the same household as patient.
Several but eligibility included starting vancomycin for 7 days before procedure and stopping day before	Both. Relapsing defined as three or more episodes of CDI or refractory disease that is unreponsive to traditional antibiotics.	Not reported	Patient identified donors-spouse, family, friend. My co-inhabit
Not reported	Recurrent disease	Not reported	Healthy volunteers

Conventional therapy with met, van and/or fidaxomicin had failed in all. Some takinh probiotics. Om average	Recurrent defined as recurrentce of diarrhoea after completion of treatment. Severe CDI defined as low	Not reported	Donors usually identified by patient. One healthy volunteer not identified by patient
Most patients received metronidazole and/or vancomycin Other antibiotics included fidaxomicin, rifaximin.	Recurrent (>2 recurrences)	Active colitis seen in 26/27 patients with pseudomembranes in 2	Healthy donors selected via thorough clinical evaluation to exclude any transmissible disease. 10 spouse, 12 son or daughter, 1 parent, 4 friends.
Metronidazole and/or Vancomycin	Relapsing and recurrent	Not reported	Spouse or close relative of good health
At least one course of adequate antibiotic therapy (>=10 days of Vancomycin at a dose of >=125mg four times a day or >=10 days of Metronidazole at a dose of 500mg three times per day). In FMT group: patients received an abbreviated regimen of Vancomycin (500mg orally four times per day for 4 or 5 days), followed by bowel lavage with 4 liters of macrogol solution (Klean-Prep) on the last day of antibiotic treatment and the suspension of donor feces through a nasoduodenal tube the next day	Recurrent	Not done	Healthy volunteers <60 years of age (faces from 15 donors were used for 43 infusions in the infusion group and for patients who had a relapse after vancomycin treatment)
Patients had a median of 4 (range, 2-16) relapses prior to study enrollment, with 5 (range, 3-15) antibiotic treatment failures of a 6- to 8-week taper with Vancomycin (95% of patients) with or without an alternative antibiotic, including Fidaxomicin (70% of participants).Patients were required to discontinue all antibiotics at least 48 hours prior to the procedure	Relapsing or recurring (having at least 3 episodes of mild-to-moderate CDI OR at least 2 episodes of severe CDI resulting in hospitalization and associated with significant modbidity	Not reported	Healthy volunteer donor: nonpregnant adults, 18-50 years of age, on no medications, with a normal body mass index
Not clear from paper, but it appears most patients had vancomycin	Refractory and recurrent	Not reported	Donors were relatives in 22 cases (73.3%) and unrelated volunteers in 8 cases (26.7%).

aracteristics	FMT characteristics		
Screening and abx cessation	**Fresh/Frozen, Route administered**	**Sample preparation Transplant sample sourcing, screening, preparation; , volume, mixing solution, storage and time from collection to transplant**	**Proceedure: Bowel Prep/Drugs used prior to FMT i.e Moviprep 2 sachets/PPI (dose), prokinetic (dose), Loperamide FMT administration Follow up method**
Within 30 days before donation (usually 7 days) screened: Blood:HAV (HAV ab (IgM and IgG), HBV (ab to HepB surface antigen and core antigen), HCV (HCV ab RIBA-II), HIV-1 & 2 (EIA), Treponema pallidum (rapid plasma reagin test). Stool: C diff (Toxin A or B (cytotoxin) detection), enteric bacterial pathogens (selective stool culture), ova/parasites (light microscopy) No antimicrobial therapy in previous 6 months	Fresh nasogastric, with tube placement on morning of transplant and tube tip placement confirmed by radiography	Stool obtained 6 or less hours prior to transplant. Approx 30g or 2cm^3 preferably soft stool selected and homogenised in 50-70ml 0.9N sterile saline (household blender - slow speed setting initially, rising gradually to maximum and continued then for 2-4 min) until sample smooth. Filtered through coffee paper filter x2 allowing adequate time for slow filtration to end.	20mg omeprazole evening before and morning of transplant. 25ml of stool suspension adminitered then tube flushed with 25ml sterile 0.9N saline. Tube removal. Normal diet and physical activites allowed immediately. Follow up by telephone or clinic visit and stool specimens examined for c.diff toxin A in most patients.
open Biome Criteria followed	Frozen pills	Not stated	Not described
no antibiotics for 6 months; stool tested for C. diff , enteric pathogens, ova and parasites, MDR gram nehgatives, MRSA, VRE; Serum tested for Hep A, Hep B, Hep C, HIV 1 and 2, strongyloides, treponema, Entamoeba. High risk lifestyle, FH of GI cancer, IBD, systemic diseases, personal GI disease	fresh via colonoscopy	Mean time from donation to infusion was 3.8 hours;mass of donation not stated but mixed with 500mls saline and blended and strained; delivered to right colon through colonoscope	2 groups FMT group received 4L of macrogol bowel cleansing solution for 1-2 days on the last 2 days of vancomycin followed by FMT. The other group had bowel cleansing and vancomycin standard treatment.

Sporicidal disinfection was performed in patient rooms as per institutional protocols; specific instruc- tions with handouts regarding sporicidal home cleaning were provided to patients to prevent reinfection.	Fresh or frozen via Colonoscopy and NG tube	Not reported	Not reported
Some tests are performed for screening: serology for hepatitis A, B and C, human immunodeficiency virus (HIV), fecal parasitology, fecal test for Clostridium difficile, and fecal culture.	Fresh via enteroscope	Mixed in N. Saline. Volume and other variables not stated	Not reported
Donors were screened for hepatitis A, B and C and HIV infection, as well as enteric bacterial pathogens including Salmonella, Shigella, Campy- lobacter and Yersinia species.	Fresh via Gastroscopy or colonoscopy	A fresh stool sample of 50–100 g was obtained from the donor on the day of the instillation procedure. The stool sample was spread out onto a gauze pad which was then placed in a strainer. The gauze was flushed with 250 ml sterile 0.9% NaCl and the resulting suspension was collected and aspirated into syringes. A flexible videogastroscope was intro- duced into the distal duodenum. Approximately 200 ml of sample solution was introduced	No bowel prep given to colonic delivered FMT

The donorshad to submit their medical records and underwent serologic testing for HIV and Hepatitis B and C, and stool testing that included screening for routine enteric pathogens, *C. difficile* toxin B, and examination for ova and parasites, and *Giardia* and *Cryptosporidium* antigens. Donors were excluded if they had GI co-morbidities or had used antibiotics within 3 months.	Fresh or frozen via Colonoscopy	Approximately 50g of fecal material was placed into a standard commercial blender (Oster, Subeam, Rye, NY) and homogenized in 250 ml of sterile, non-bacteriostatic normal saline. Faceal suspension, if stored , was put in 10% glycerol and stored at -80 for up to 8 weeks. The frozen preparation was diluted in 250ml salne before infusion.	Patients were maintained on full dose of vancomycin (125mg, four times daily by mouth) until 2 days before the FMT proce- dure. The day before the procedure, the patients were prepped using a split dosage polyethylene glycol purge (GoLYTELY or MoviPrep), which is standard in our endoscopy unit, before colonoscopies to wash out residual antibiotic and fecal material.
Not reported	Oral capsules vs colonoscopy	Not reported	Not reported
Blood was screened for hepatitis B surface antigen, hepatitis C antibody, Helicobacter pylori and syphilis serologic markers, human immunodeficiency virus types 1 and 2, and human T-lymphotropic virus types I and II. Stool was processed for enteric bacterial pathogens, C difficile toxin, and ova and parasites.	Retention enema	Approximately 150 g of fresh stool collected was emulsified in 300 mL of sterile water. The supernatant component was administered rectally by en- ema.	All CDI therapy was discontinued at least 24 hours prior to FT.
no antibiotics in preceding 90 days; blood for HAV, HBV, HCV, HIV 1&2, Treponema pallidum; stool for culture for bacteria, stain for ova and parasites, C. diff. toxin A and B	Fresh via colonoscopy	stool obtained 6 hours or less prior to transplant6=8 tablespoons of donor stool added and shaken in 1litre of sterile water passed through gauze. Aliquoted in 60ml syringes.	polyethelene glycol bowel prep night before transplant; 500-960mls administered via scope mainly to rightcolon; Avoid defecating for 30-45 mins

Not reported	fresh or frozen not stated; 12 of 16 centres used colonoscopy route	Not reported	prep not stated; questionnaire sent out to 16 centres to retrospectively collect data; method of follow up at each centre not stated but had to have data for at least 12 weeks to be eligible for inclusion
Testing for HIV-1 and HIV-2 was performed within 2 weeks before donation for FMT. Other serologic and stool testing was performed within 1 month before FMT and included testing for hepatitis A, B, and C viruses; testing for Treponema pallidum; polymerase chain reaction (PCR) testing for detection of C difficile toxin; culture for enteric pathogens (Esch erichia coli, Salmonella, Shigella, Yersinia, Campylobac- ter, Listeria monocytogenes, Vibrio parahaemolyticus, and V cholerae); testing for fecal Giardia and Cryptosporidium antigens; acid-fast stain for detection of Cyclospora and Isospora; ova and parasite testing; and enzyme immunoassay for detection of Rotavirus.	Fresh via colonoscopy	The protocol specified a “dose” of 100 g of stool diluted in 500 mL of nonbacteriostatic 0.9% normal sa- line immediately before the procedure, but the study relied on fresh stool, which has unpredictable weight and volume, and most provided specimens were less than 100 g.	Donors took an osmotic laxative (magnesium hydroxide) the evening before and provided fresh stool the day of FMT. All donor specimens were transported on ice and processed within 6 hours of collection. Patients were given a standard bowel purge (sodium sul- fate, potassium sulfate, and magnesium sulfate oral solution) the evening before the procedure. For patient convenience, sodium sulfate, potassium sulfate, and magnesium sulfate oral solution was substituted for the polyethylene glycol (PEG) bowel purge described in the study protocol.

no antibiotics for 3 months; stool tested for C. diff toxin PCR, enteric pathogens, ova and parasites, Cryptosporidium, Microspora; Serum tested for Hep A, Hep B, Hep C, HIV 1 and 2; H. pylori' Human T lymphotropic virus	fresh via colonoscopy	stool obtained within 30 mins of transplantation; 50g of stool into 200mls of saline and blended; Aspirated into single 60ml syringe for delivery	4 litres polyethelene glycol bowel prep; 60mls administered via scope into right colon; follow up combination of clinic, telephone and questionairres
no antibiotics for 3 months; stool tested for C. diff , enteric pathogens, ova and parasites; Serum tested for Hep A, Hep B, Hep C, HIV 1 and 2; CMV, EBV, high risk behaviours, systemic antineoplastic drugs, immunosuppressives, history of GI disease. Directed donors to avoid foods which recipient may be allergic to for 5 days prior.	fresh via NGT	time from collection to transplant not stated; 30g stool added to 100mls saline and blended;filtered throgh gauze; 30-60mls infused	8.5g-17g polyethylene glycol in 8oz of water 3 times a day for 2 days prior to FMT; omeprazole 1mg/kg orally day before and on day of FMT; follow up all patients called 2 days after FMT, further follow up combination of clinic, telephone and repeat C. diff. testing
no antibiotics for 6 months; stool tested for C. diff , enteric pathogens, ova and parasites, norovirus,enterovirus; Serum tested for Hep A, Hep B, Hep C, HIV 1 and 2, human lT-cell ymphotrophic virus 1&2, treponema	retention enema	time from collection to transplant not stated; 150g stool added to 300mls water and homogenised with spatula 100mls infused	no bowel prep stated;100mls infused via enema;follow up methods not stated but retrospective analysis extracted from clinical record
Questionnaire. Pathogens, HIV, HABC, CMV, EBV, syphilis, strongyloides, entamoeba. Screening every 4 months	Fresh and Frozen. Lower GI route	100g of stool homogensied and mixed in 300mls of water. If frozen kept for 30 days at -20C. If fresh administered within 24hrs.	Nil

Within 30 days before donation (usually 7 days) screened: Blood:HAV (HAV ab (IgM and IgG), HBV (ab to HepB surface antigen and core antigen), HCV (HCV ab RIBA-II), HIV-1 & 2 (EIA), Treponema pallidum (rapid plasma reagin test). Stool: C diff (Toxin A or B (cytotoxin) detection), enteric bacterial pathogens (selective stool culture), ova/parasites (light microscopy) No antimicrobial therapy in previous 6 months	Fresh via NGT	time between stool collection and transplant not stated; 30g of stool blended with 150mls saline and filtered; 30mls infused via NGT	no bowel prep stated;30mls infused via NGT;omeprazole given prior to FMT; follow up methods not stated but retrospective analysis extracted from clinical record
No antibiotics for 6 months. Blood for FBC, CRP, protein,creatinine, LFTs, HBV, HCV, HIV 1 &2, treponema. Stools for Cdiff, pathogens, OCP,	Fresh, within 6 hours colonoscopic	Stool obtained 6 or less hours prior to transplant. Homogenised in 100-200ml water.	Colonic lavage ith 4l PE solution.
No antibiotics for 3 months. Excluded chronic gastrointestinal condirions, active peptic ulcer disease, GERD, IBS,IBD,polyps, mlaignancy. Blood for HABCV, HIV, Treponema, stool for culture, OCP, cryptosporidium, microsporidia, Cdiff	Fresh, colonoscope	Donors given 30ml MgOh evening before donation. Stools within 6 hours of passage blended with 100ml Nsaline and sieved for delivery.	Bowel prep for colonoscopy (not stated which), 4mg operamide either before or after FMT
High risk behaviours, no antibiotics for 3 months, Blood for HIV, HABC, STDs, stooll for bacterial culture, OCP, Cdiff	Fresh, colonoscope (11); 1 nasoduodenal	Donor given mg citrate before. stool collected within 6 hours of preocedure. 6-8 tablespoons to 1l tap water, shaken.	PEG bowel prep, 400-500 ml to TI/Right colon. Patients given 2 tablets of diphenoxylate/atropine. A week later 2 month course of Saccharomyces boulardii

3 unscreened. High risk behaviours, antibiotics in 3 months, blood for HIV, HABC, terponema, stool for Cdiff, bacterial culture, OCP, Giardia, Cryptosporidium,	Fresh, colonoscope	Time between donation and colonoscopy not stated	On day of treatment patients given 2 imodium tablets 2 hours prior and 1 after. Bowel prep not recorded.
Selective based on discretion. Blood from some for viruses (HABC, HIV), stool from some for Cdiff and enteric pathogens	Fresh colonoscope	Time between donation and colonoscopy not stated	PEG bowel prep. Some (not clear how many) had 2 immodium immediately after and then again6 hours after FMT
Screened for occult infectious conditions and no abx use in preceeding 3 months	Fresh, Upper GI (NG or PEG)	30 g of donor stool in mixed in saline. 25mls given in an infusion.	Pre-treated with 3 days of vancomycin and proton pump inhibitor prior to procedure
No significant medical history, no antibiotics for prior six months. Donor feces were screened for enteric pathogens and blood was screened for antibodies to hepatitis A, B, and C; HIV; and Treponema pallidum within 2 weeks of donations	Fresh: 26 patients; Frozen: 23 patients. Administered by colonoscopy	30g of stool in 200mls of saline or glycerol. If frozen stored in -80C for up to 16 weeks.	Polyethylene glycol prior to procedure
Not reported	Fresh, both routes	Not reported	Not reported
Donor feces were screened for enteric pathogens and blood was screened for antibodies to hepatitis A, B, and C; HIV	Fresh via colonoscopy	Stool collected morning of transplant, filtered and mixed with saline. 250 - 400mls infused into patient.	Abx stopped 3 days prior to FMT

Age range 18-50 years, BMI 18.5 - 25. No significant medical history, not pregnant, no antibiotics for prior six months. Donor feces were screened for enteric pathogens and blood was screened for antibodies to hepatitis A, B, and C; HIV; and Treponema pallidum within 2 weeks of donations. Donors refrain from common allergens for 5 days before donation.	Capsule (oral) frozen for mean of 113 days (range 30-252 days).	Each inoculum was prepared from the feces of a single donor. The final slurry was concentrated by centrifugation and resuspended in saline at one-tenth the volume. Fecal matter solution was pipetted into size 0 capsules (650 µL), which were closed and then secondarily sealed in size 00 capsules. Capsules were stored frozen at −80°C (−112°F) till use. A full treatment of 30 capsules contained sieved, concentrated material derived from a mean of 48 g of fecal matter (mean per capsule, 1.6 g; range, 1.0-2.05 g). Samples stored for 4 weeks without use to allow for retesting for HIV, hep B and C. (full screening and exclusion details given in appendix)	Abx stopped 48 hrs prior to FMT
Donor feces were screened for enteric pathogens and blood was screened for antibodies to hepatitis A, B, and C; HIV	Fresh. Upper GI in 13 patients, lower GI in 1 patient	Fresh stool sample (30–50 g) homogenized and mixed with water. About 120–180 ml of the suspension was instilled through NGT; 300–500 ml was administered if IMT was done via colonoscopy.	Abx stopped 24 hrs prior to FMT and given proton pump inhibitor prior to procedure
Excluded if abx within preceding 3 months. Exclusion criteria also included immunosuppressive agents, including chemotherapeutic agents; had known or recent exposure to HIV,hepatitis B or C;had a current communicable disease; participated in high-risk sexual behaviors; used illicit drugs; had a history of incarceration; traveled within 6 months to areas with endemic diarrheal illnesses; or had history of infl ammatory bowel disease, irritable bowel syndrome or chronic diarrhea, gastrointestinal malignancy or polyposis). Blood tested for HIV, Hep A/B/C and stool for OCP and giardia antigen and cryptosporidium	Fresh (within 8 hours), colonoscopy	Suspended in saline, mixed by hand or blender, filtered and infused as 300 to 700 mls	Abx stopped 48 to 72 hrs prior to FMT. Bowel prep given before procedure
no abs for 3 months. No laxatives, hstory of constipation, no history of GI disease, travel in 3 months, not on immunosuppressives or chemo. No metabolic syndrome, autoimmune, atopic disease	Fresh (within 6 hours), colonoscopy	Fresh in blender 500ml Nsaline, strained. 60ml drawn up in 8-9 syringes per patient.	Abs stopped prior to procedure.
screening as per FDA guidelines 2011	Frozen stool (> 2 months in 16 patients and <2 months in 4 patients), colonoscopy route in 19, jejunal	30g in 120ml N.saline, divided into 50ml aliquots	Not reported

Excluded if "history of antibiotic use" (time not specified), high risk behaviour, prisoners, GI disease,	Fresh. Initial FMT in 118(81%) colonoscope, 13(9%) OGD, 3(2%)	Milk of magnesia to donors. 60-100g stool suspended in 300-500ml nsaline, mixed, sieved. 75-200ml for upper route (OGD, enteroscopy), 250-400ml colnoscopically,	Bowel prep given. Loperamide after FMT
Blood and stool screened for transmissible diseases	Fresh, given via a combination of jejunal and colonic route	25-30g of stool given as 180mls via enteroscopy and 270mls via colonoscopy	Not mentioned
Potential donors were accepted only if serum antibodies against HIV 1 and 2, hepatitis C virus, and hepatitis B surface antigen were negative, as were stool cultures for Salmonella, Shigella, Campylobacter, enterohemolytic Escherichia coli, and Clostridium	Fresh, given as enema (lower GI	50g of fresh faeces prepared in an anaerobic cabinet by adding and stirring small portions of pre-reduced and pre-warmed (37 °C) sterile isotonic saline, to a total of 500 ml.	Not mentioned
Questionnaire adressing risk factors for potencially transmissible diseases. Donor feces were screened for parasites, including Blastocystis hominis and Dientamoeba fragilis; C.difficile, and enteropathogenic bacteria. Blood was screened for HIV; human T-cell lymphotropic virus types 1 and 2; hepatitis A,B, and C; cytomegalovirus; Epstein-Barr virus; Treponema pallidum; Strongyloides stercoralis; and Entamoeba histolytica. A dnor pool was created, and screening was repeated every 4 months. Before donation, another questionaire was used to screen for recent illnesses.	Fresh via nasoduodenal tube	Feces were collected by the donor on the day of infusion and immediately transported to the hospital. Feces were diluted with 500mls of sterile saline 0.9%. This solution was stirred, and the supernatant strained and poured in a sterile bottle. A mean (+-SD) of 141+-71g of feces was infused. The mean time from defecation to infusion was 3.1+-1.9 hours	Bowel lavage with 4 liters of macrogol solution (Klean-Prep) on the last day of antibiotic treatment. Within 6 hours after collection of feces by the donor, the solution was infused through a nasoduodenal tube (2 to 3 minutes per 50mls). The tube was removed 30 minutes after the infusion, and patients were monitored for 2 hours. Patients kept a stool diary and were questioned about stool frequency and consistency, medication use, and adverse effects. Stool tests for C.difficile toxin were performed on days 14,21,35, and 70 and whenever diarrhoea occured.
Volunteers were excluded for any significant past medical history or any use of antibiotics in the preceeding 6 months. Initial screening using the American Association of Blood Banks donor questionaire for exposure to infectious agents. Physical examination and general laboratory screening tests (within 30 days of donations). All results had to be within normal range for age and sex. Donor feces were screened for enteric bacterial	Frozen via colonoscopy or NGT	Donors were asked to take a dose of milk of magnesia the day before fecal collections to facilitate manipulation of the sample. A fecal suspension was generated in normal saline without preservatives, using commercial blender. Materials were passed through 4 sieves to remove particulate material. The final slurry was concentrated 3-fold by centrifugation and then resuspended in sterile saline with 10% glycerol added as a bacterial cryoprotectant. Inocula were then frozen at -80 C pending use. Each sieved inoculum was calculated to have been derived from approximately 41g of fecal material. Inocula were stored frozen for up to 156 days, range, 29-156 days; frozen material was thawed in a 37 C water bath, and then kept on ice until delivery.	Subjects assigned to colonoscopic administration underwent a standard bowel preparation with 4 liters of PEG solution, followed by endoscopic administration to the right colon of 90 cc thawed inoculum:further diluted to 250cc for adults and 160 cc for paediatric patients. Patients were given a single oral dose of loperamide at the time of procedure. Subjects assigned to NGT delivery of FMT were
Pre-medical examination was carried out with a questionnaire in order to rule out high-risk individuals (such as drug use, promiscuity, known illness, taking antibiotics or trips abroad in the past six months). Stool samples	Fresh stool delivered via nasogastric route in 15 patients and nasoduodenal route in 15 patients	60 grams, it was placed in 200 mL of mortar physiological saline (0.9%) and harvested. then the homogenate of 4 × 4 cm was filtered sterile gauze pads transferred to another vessel and finally were taken from the filtrate up to 100 ml syringe and given to patient within 6 hours.	Antibiotics were stopped prior to transplant and patients were given laxatives. Patients received both metoclopramide and high dose proton pump inhibitor on the day of the transplant.

Total no of infusions	Define primary outcome
not explicitly stated. Data implies a single infusion on a single occasion for each patient	Not explictly stated, but authors report outcome based on symptom resolution and / or CDI toxin negativity
NA	Clinical resolution of diarrhoea at 8 weeks
13/20 had 1 FMT; 6/20 had co-existent PMC and received infusions every 3 days until symptom resolution (4 had 2 infusions, 1 had 3 infusions and 1 had 4 infusions	Resolution of diarrhoea 10 weeks after the end of the treatments

Not reported	Early Failure rate defined as non-response or recurrence of diarrhoea with either toxin or PCR positive CDI within 1 month of FMT
1 infusion via enteroscopy	not defined in paper but implied symptom free to end of follow up
I infusion via gastroscopy or colonoscopy	successful treatment defined as no further contact with the clinic due to CDI symptoms within 80 days of FMT

4 of 43 had repeat infusion	Not specified
1 infusion via colonoscopy or 1 course of capsules.	Defined as cure but no time period given
Five patients underwent a second FT because of ongoing diarrhea; 3 had symptom resolution and 2 continued to experience diarrhea despite 2 FTs.	resolution of symptoms- no time period defined
not explicitly stated but imples single infusion for all patients	Prevention of further CDI relapse and/or significant diarrhoea requiring vancomycin; time frame for outcome not stated

78 patients had single infusion; 12 patients had 2 infusions	response defined as absence of diarrhoea or marked reduction in stool frequency and without need for further antibiotics within 12 weeks after 1 or more FMTs
1 infusion via colonoscopy	Resolution of diarrhoea without need for anti CDI therapy during 8 week follow up

18 had single infusion; 2 had 2 infusions	Resolution of diarrhoea without recurrence of symptoms within 3 months of FMT
9 patients had single infusion, 1 patient had 2 infusions	Not defined in paper but implied symptom free to end of follow up
if no resolution of diarrhoea after 7 days post FMT then further enema give. Range given 1-10(46/94 had 1 FMT, 20/94 had 2 FMT, 17/94 had 3 FMT, 11/94 had 4 or more)	Cured following FMT if no recurrence of diarrhoea at 6 months follow up
1, if no response at day 4, then further FMT and if no response then FMT or abx. Primary outcome based on up to 2 FMTs.	Clinical resolution of diarrhea without relapse at 13 weeks

14/15 had 1 FMT;1/15 had 2 FMT	Not explicitly stated but implied that "cure" was no symptoms at follow up after 1 FMT
67 had 1; 3 had 2	Resolution diarrhea without a positive C difficile toxin stool test at 12 weeks
28 had 1; 3 had 2	Not defined.
1 infusion in all but 1 patient who had repeat via ND route	No strict definition. Authors state : 'A successful treatment was determined by the resolution of diarrhea, a fall in white cell count, or absence of fever and an improvement in vital signs'.

1	Resolution defined as positive stools after FMT.
1	not defined in paper but implied symptom free to end of follow up
1	Resolution of diarrhea without recurrence within 60 days of FMT
1	Resolution of diarrhoea with a negative C. difficile toxin stool test at 3 months
1 infusion in 27 patients, multiple infusions in 4 patients	Resolution was defined as the absence of significant diarrhea (diarrhea as defined by at least three episodes per day) or a marked reduction in diarrhea not requiring antibiotic therapy.
1	Clinical response was defined as absence of diarrhea, cramps, and fever within 3 to 5 days of transplant

N/A	Response defined as less than 3 bowel movements in 24 hrs
1 in 10 patients, 2 in 2 patients, and 3 in 2 patients received three FMTs	Defined as less than 3 loose bowel movements a day for 2 consecutive days after FMT and no need for further CDI therapy on day 7.
1 infusion in 75 patients, 2 infusions in 2 patients	Resolution without recurrence within 90 days including those that needed a second infusion or antibiotics
1 infusion	Primary outcome not defined
1 infusion in 17 patients, 2 infusions in 3 patients	Resolution of diarrhoea and/or absence of CDI toxin in stool as measured by PCR after at least 3 months follow up

146 had one infusion, 12 out of 25 early recurrences had another	Initial Resolution of CDI symptoms with no recurrence after 12
1	Resolution of diarrhoea and disappearance of stool Cdiff toxin
1 in 22 patients and 2 in 1 patient	Resolution of diarrhoea in 3 days with no recurrence in 3 months
16 patients had 1 infusion; 3 who did not respond in this group had 2nd infusion.	Cure without relapse within 10 weeks after the initiation of therapy. For patients in the infusion group who required a second infusion of donor feces, follow up was extended to 10 weeks after the second infusion. Cure was defined as an absence of diarrhoea or persisent diarrhoea that could be explained by other causes with three consecutive negative stool tests for C.difficile toxin. Relapse was defined as diarrhoea with a positive stool test for C.difficile toxin.
20 patients in both study arms had one infusion (14 was cured after the first infusion (70%)). One patient in the NGT arm refused subsequent retreatment. The ramaining 5 patients were given a second infusion (4 patients obtained cure after second infusion, resulting in an overall cure rate of 90%).	Clinical resolution of diarrhoea off antibiotics for C.difficile, without relapse within 8 weeks. For patients who required a second treatment dose, a follow-up was calculated starting at the time of the second administration.
1 infusion in 27 patients and 2 infusions in 3 patients.	Primary cure rate was defined as resolution of symptoms without recurrence within 6 weeks after a single FMT, while secondary cure rate was calculated

	Results
Flow/loss of patients **Response definition** **Data on each response definition (and definition of demoninator) %** **Notes**	**Outcome 1 infusion**
Overall response rate: 15/16 (94%). Pretreatment vm eliminated or reduced diarrhoea in most patients. 1/19 patients had missing documentation 2/18 patients died 14/16 patients submitted post transplant stool samples (20 samples total). The two non-submitted appeared to be diarrhoea free (upto 90 days). Response definition: c diff toxin negative. 13/14 had negative stool test for c.diff toxin 1/14 had relapse and positve c.diff toxin stoll test 17 days post transplant. Therefore response rates are: 92.9% (13/14) for those submitting a stool sample 81.2% (13/16) for those followed up who were still alive; with those not submitting a stool sample assumed worse case (ie. c diff. toxin positive) 81.2% (13/16) for those who provided a sample or died (assumed worse case- ie. c diff toxin positive) 72.2% (13/18) assuming those who died or did not submit a stool sample were worse case (ie. c diff. toxin positive). 68.4% (13/19) assuming those who died or did not submit a stool sample or had missing documentation were worse case (ie. c diff. toxin positive) As pateints were pre-treated with vm study authors state "*It was not possible to differentiate between patients whose colitis resolved as a result of their pretransplantation course of vancomycin and those with colitis improved as a result of stool transplantation itself*" although patients had previously had multiple ab treatments without overal success. There were no episodes of post-transplantation diarrhoea among the the 15 patients (c diff negative or non samply supplying) who survived the 90 day follow-up period. (unclear statement: not sure what total follow up period was after 90 days or whether this means during the 90 days).	15/16 (94%)
7/9 (77%) high dose and 7/10 (70%) low dose diarrhoea free at 8 weeks. Of the 5 non-responders 4/5 (80%) cured with high dose re-challenge. -94% secondary cure rate	NA
Primary end point defined as resolution of diarrhoea associated with C. diff infection 10 weeks after the end of treatment; in FMT group 18/20 (90%) achieved primary end point; In vanc group 5/19 (26%)patients achieved primary end point	13/20(65%)

Breakdown cure rates from both derivation and validation cohorts: recurrent CDI - 357/403 (89%), severe CDI 10/40 (25%), severe-complicated CDI 8/19 (42%). Total cure rate 375/462 (81.2%)	not reported
12 patients treated but 6 month follow up only available for 11. Response rate 10/11 (91%) in patients with full follow up. Response rate 10/12 (83%) in all patients treated. In only one of 11 cases did the bacterial infection relapse, after a new cycle of antibiotic therapy to treat an urinary tract infection, without diarrhea.	10/12 (83%)
A total of 33 of 40 treatment episodes (83%) were successfully treated with FMT. In 29 of 40 treatments (73%) the first treatment was successful, with no documented recurrence of diarrhoeal disease within 80 days. Of the 11 patients failing to respond to the first instillation treatment, 6 patients received a second instillation, 4 of which were successful. Initially 38 patients given FMT via gastroscope (response to single infusion 28/38 (74%)) and 2 patients given FMT via colonoscopy (response 1/2 (50%)). 11 non-responders 6 were given 2nd FMT responses 3/4 (75%) via gastroscope and 1/2 (50%) via colonoscope	29/40 (73%)

The overall rate of infection clearance was 41/43 (95%), as evidenced by symptom resolution and negative PCR testing for *C. difficile* toxin B after 2 months of follow-up. Response rate from fresh FMT was 11/12 vs 19/21 from frozen FMT	37/43 (86%)
Overall response rate: 41/43 (95%). Cure rate colonoscopy group 21/21 (100%) and 20/22 (91%) in capsule group.	41/43 (95%)
After FMT, 25 of 27 (93%) experienced clinical resolution. Of these, 22 resolved within 24 hours of transplant. Five patients underwent a second FMT because of ongoing diarrhea; 3 had symptom resolution and 2 continued to experience diarrhea despite 2 FMTs.	22/27 (81%)
26 sequential patients follow up and analysis available for all. 24/26 (92.3%) achieved primary outcome;	24/26 (92.3%)

82 patients met inclusion criteria but analysis based on results of 80 patients as 2 lost to follow up (2 deaths so no 12 week follow up data fro these patients and excluded from final analysis); 80 patients in 16 centres had FMT for CDI with co-existing immunocompromise (36 IBD and on immunosupression, 19 solid organ transplants, 3 HIV/AIDS, 7 cancer and treatment with chemo, 15 chronic illness); response defined as absence of diarrhoea or marked reduction in stool frequency and without need for further antibiotics within 12 weeks after 1 or more FMTs; cure after 1 infusion 62/80 (77.5%); cure after 2 infusions 70/80 (87.5%); if 82 patients included in analysis cure after 1 infusion is 62/82 (75.6%) or 2 infusions is 70/82 (85.3%)	62/80 (77.5%)
In the intention-to-treat analysis, 20 of 22 patients (90.9%) in the donor FMT group achieved clinical cure com- pared with 15 of 24 (62.5%) in the autologous FMT group (P = 0.042). Resolution after autologous FMT differed by site (9 of 10 vs. 6 of 14 [P = 0.033]). All 9 patients who developed recurrent CDI after autologous FMT were free of further CDI after subse- quent donor FMT. Direct clinic follow up at 2 and 8 weeks	20 / 22 (90.9%)

20 patients analysed; Response defined as primary cure rate- no recurrence of symptoms of diarrhoea within 3 months of single FMT infusion; secondary cure rate was defined as no recurrence of symptoms within 3 months after2 infusions of FMT; 9/9 community aquired CDI had single infusion with cure rate of 100%; 9/11 Hospital aquired CDI had single infusion with cure rate of 82%; 2 patents in the hospital aquired group had second infusion and cured so secondary rate in this group was 100%	18/20 (90%)
10 patients; response not explicity defined but appears to be resolution of infection (how this determined is not stated); 9/10 had resolution, 1/10 had further FMT after relapse at 2 months following course of antibiotics.	9/10 (90%)
94 patients in total given FMT; response defined as no diarrhoea for 6 months post FMT; overall response to FMT alone was); 5/94 patients received responded to FMT and vancomycin combination giving a further increment in cure of 5.3%, giving an overall cure rate of 91.5%;8 patients did not respond to FMT of which 6 died and included as FMT failures; 11 patients received 4 or more FMTsNB the authors state this cohort is an expansion of previously published series by Lee et al 2011 which included the same first 27 patients (are we double counting this?)	45/94 (47.9%)
Overall response as per primary outcome - up to two infusions (ITT) - 159/219 (73%).	113/219 (52%)

11/15 were diarrhoea free during follow up of median 16 weeks (range 4 to 24 weeks). Follow up period not used to define response; Response rate 73.3% calculated on being diarrhoea free at follow up after single infusion	11/15 (73%)
Resolution of symptms during 12 weeks follow up in 66/70 (94%). 34/34 (100%) in non-027 CDI; 32/36 (89%) in 027-CDI. Of the 4 027-CDI all died 1.5-3 months after. One who refused colectomy, two of CDI, one with myelome reated uraemia. This patient was retreated with antbiotics for pneumococcal septicaemis and menignitis after 1st FMT	63/70 (90%)
Of the 30 patients who had diarrhoea 29/30 (97%) had improvement or resolution of diarrhoea. Median time to imrpovement 3 days. At 3 months 91% (21/23) had maintained improvement or resolution. Of those who had 2 2 had subtotal colectomies and second FMT via upper OGD. All three improved in 5 days; one had a recurrence.	26/30 (87%)
Overall cure rate: 12/12 (100%).	11/12 (92%)

20/20 (100%)	20/20 (100%)
19/20 (95%) responded to first treatment remaining symptom free for follow up of 6 months to 5 years. The one patient who did not respond was retreated after 5 months with same donor-immediately successful -so secondary cure rate 100%. 3 patients represented at 4months-6 years after but these were re infections following repeat treatment with antibiotics	19/20 (95%)
Overall response rate: 59/75 (79%). Response rate if patients only included if primary outcome and negative CDI toxin post FMT: 57/75 (76%). Secondary cure rate (patients failed FMT, but subsequently resolved diarrhea after a course of oral vancomycin): 68/75 (91%).	59/75 (79%)
Overall response rate: 47/49 (96%). Other response rates: FMT with fresh faeces, individual donor: 14/15 (93%). FMT with fresh faeces, universal donor: 11/11 (100%). FMT with frozen faeces, universal donor: 22/23 (96%).	47/49 (96%)
Overall response rate 27/31 (87%). If given via upper GI route 3/9 (33%). If given via lower GI route (including those that didn't respond to upper GI route) 24/28 (85%).	24/31 (77%)
Overall response rate 12/12 (100%). If exclude pre-transplant CDI toxin negative patients: 9/9 (100%)	12/12 (100%)

Overall response rate 18/20 (90% (95%CI 68-98%)) at 8 weeks. Initial response rate 14/20 (70%), those who failed retreated after average of 7 days.	NA
Overall response rate 11/14 (79%). 8 remained cured at 100 day follow up (3 deaths from underlying cancer).	8/14 (57%)
70/77 (91) met primary outcome at 90 days.	70/77 (91%)
20/22 (91%%) responded at 3 months. 2 that relapsed had a further infusion (one by upper GI route) with both responding	19/22 (86%)
20/20 (100%) overall response rate	17/20 (85%)

Initial Resolution of CDI symptoms with no recurrence after 12 weeks-121/146. 25 developed recurence within 12 weeks. 12 had more than 1 FMT but with antibiotics therefore not included in the analysis	121/146 (82.9%)
27/27 (100%) at 1-3 month after FMT.	27/27 (100%)
Overall response rate: 16/23 (70%)	15/23 (65%)
The primary end point was cure without relapse within 10 weeks after the initiation of therapy. For patients in the infusion group who required a second infusion of donor feces, follow up was extended to 10 weeks after the second infusion. The secondary end point was cure without relapse after 5 weeks. Cure was defined as an absence of diarrhoea or persistent diarrhoea that could be explained by other causes with three consecutive negative stool tests for *C.difficile* toxin. *Relapse was defined as diarrhoea with a positive stool test for* C.difficile *toxin.* An adjudication committee whose members were unaware of study-group assignments decided wchih patients were cured.	13/16 (81%)
The primary endpoint was clinical resolution of diarrhoea off antibiotics for C.difficile, without relapse within 8 weeks. For patients who required a second treatment dose, follow-up was calculated starting at the time of the second administration. Resolution of diarrhoea was defined as <3 bowel movements per 24 hours. Secondary endpoints included improvement in subjective well-being per standardized questionaire and presence of adverse events.	14/20 (70%)
With the use of the nasogastric tube, the primary and secondary cure rate was 80% and 93.3%, respectively. When given via nasoduodenal route, the primary cure rate was 100%. This results in an overall primary cure of 90.0% and a secondary cure rate of 96.7%.	27/30 (90%)

1 or more infusions	Total follow up period	Adverse events - mild	Adverse events - serious	1.Were selection/eligibility criteria adequately reported?
15/16(94%)	90 days post transplantion, assessed by examination of medical records.	no mention	2 patients died between transplant and follow up stool testing for c.diff toxin. One had end stage renal disease and was receiving peritoneal dialysis. Developed peritonitis 3 days post transplant and died shortly after. The second patieint died 14 days post transplant of pneumonia complicating COPD and atherosclerosis (study authors state: *"the possibility that the use of the nasogastric tube contributed to the peritonitis cannot be excluded"*)	yes
19/20 (95%)	Not reported	None reported	none reported	yes
18/20(90%)	primary end point 10 weeks after end of treatment	none in vanc group; FMT group 19/20 had transient diarrhoea, 12/20 had abdominal pain and bloating	2 deaths in FMT arm	yes

375/462 (81.2%)	3 months	Not reported	Not reported formally	yes
10/12 (83%)	6 months	Not reported	None	yes
33/40 (82.5%)	80 days	Not reported	5 deaths; The remaining 5 patients had serious co-morbid conditions and died 3 weeks–2 months after the FDIT procedure. Two of these 5 patients were seriously weakened after long lasting diarrhoeal disease, 1 being the oldest patient in the series (94 y). Additionally, 1 patient had advanced stage Wegener's granulomatosis with complications, 1 patient had acute myelogenous leukaemia requiring repeated antibiotic treatment for other infections, and 1 patient with advanced cardiovascular disease developed fulminant colitis and underwent subtotal colectomy, and subsequently died of complications.	yes

41/43 (95%)	12 months	Not reported	Not reported	yes
41/43 (95%)	Not specified	Transient nausea and vomiting	None	yes
25/27 (93%)	mean follow-up at 427.3 days after transplant.	Not reported	Not reported	yes
24/26 (92.3%)	follow up mean 10.7 months ranged from 2-30 months	mild diarrhoea post FMT in 3 patients	no serious adverse events	yes

70/80 (87.5%)	minimum of 12 weeks required; mean follow up 11m (range 3-46m)	self limited diarrhoea in 3, fever in 1, bloating and abdo discomfort in 3, hip pain in 1, Crohn's flare in 1, Pertussis in 1, nausea in 1, minor mucosal tear at colonoscopy in 1	deaths- 1 due to pneumonia, 1 due to aspiration at time of colonoscopy; hospitilisations- 1 due to fever and encephalopathy, 1 due to abdo pain after FMT, 3 due to IBD flare, 1 colectomy, 1 hip fracture, 1 influenza, catheter infection	yes
21 / 22 (90.9%)	8 weeks for efficacy, 6 months for safety	Chills were reported more frequently after autologous than donor FMT (P = 0.053). Rates of other solicited AEs (fever, abdominal pain, bloating, nausea, vomiting, diarrhea, flatulence, anorexia, and constipation) did not differ significantly between groups.	There were no SAEs related to FMT.	yes

20/20 (100%)	minimum of 6 months (range not stated)	self limited diarrhoea in 4; abdominal pain in 3; nausea in 2; fatigue 13	none stated	yes
10/10 (100%)	median duration of follow up 44 days (range 13-700 days)	vomiting post FMT in 1; mucoid stools for 2 days after FMT	none stated	yes
81/94 (86.2%)	6-24 months	10% had transient constipation and flatulence post FMT	6 deaths due to critical illness, not felt to be due to FMT or CDI directly but these 6 are included in the 8 who failed to respond overall	Yes
193/219 (88.1%)	13 weeks	Transient diarrhoea (70%), abdominal cramps (10%), nausea (5%) in 24 hours post FMT; constipation (20%) and flatulence (25%) in follow up period	19 deaths in total 13 week study period (unrelated). 12 patients required hospitalization because of ilnesses unrelated to FMT	Yes

12/15(80%)	median 16 weeks (4 weeks to 24 weeks) not predefined	none	none stated	Yes
66/70 (94%)	1 year. 4 with initial favourable response had replase after receiving antibiotics. 2 of these were successfully treated with FMT; 2 with recurrent antibitics for CDI	None reported	None related to FMT	Yes
29/30 (97%)	1 year 6 out of 6 maintained imrpovemement	Not reported	Micro-perforation but not related to FMT. One death at 3 months afer due to ,metastatic pancreatic cancer.	Yes
12/12 (100%)	No recurrences within 90 days of FMT. Total follow up from 2 to 29 months	None reported	None related to FMT	Yes

20/20 (100%)	Follow up mean 3 months (range 0-10)	1 pain/nausea after colonoscopy, 1 continued diarrhoea (CDIFF neg) ? Bile salt malabsorption after cholecystectom, 2 transient bloat/ cramps	1 perforation related to colonoscopy sealed with clip	Yes
20/20 (100%)	6 months to 5 years	None reported	none reported	Yes
59/75 (79%)	60 days	None	None	Yes
47/49 (96%)	All followed up for 12 weeks and 42 patients followed up for 1 year	Mild transient fever in 2 (frozen FMT)	3 deaths (unrelated)	Yes
27/31 (87%)	Mean 9 months (range 2–24)	Worsening arthritis, constipation, diarrhoea, urinary tract infection.	5 deaths; not attributed to FMT. Stroke, myocardial infarction, aspiration pnuemonia, hospitalisation for CDI not as a consequnce of FMT.	Yes
12/12 (100%)	3 weeks to 8 years	Not reported	None	Yes

18/20 (90%)	Primary outcome based on 8 weeks however patients followed up for 6 months	Transient abdominal cramping and bloating in 6 patients (30%) that resolved in 72 hours	1 hospitalised with a documented relapse of severe CDI after taking 15 capsules but had successful treatment after receiving the remaining 15 capsules after discharge. No other severe adverse events (grade 2 or above).	Yes
11/14 (79%)	100 days	Not reported	4 deaths within 30 days of FMT unrelated to FMT.	Yes
70/77 (91%)	Minimum 90 days, but median 17 months	None reported	4 patients reported a new medical condition after FMT (peripheral neuropathy, Sjogrens, ITP and rheumatoid arthritis	No
21/22 (95%)	Range 2 weeks to 17 months with ave length 3 months	pain in one patient	none	No
20/20 (100%)	Minimum 3 months (but up to 14 months)	None	None	No

121/146 (82.9%)	mean follow up 12.3 (range 1-48) months	CDI-negative diarrhoea in 7(4.8%) and constipation in 4(2.7%)	within 12 weeks-6 hospitalizations due to CDI and/or FMT. One debilitated	No
27/27 (100%)	Ranged from 9.7 -34 months (mean 20.6 months)	Low grade fever (18.5%) and bloating (11.1%)	None	Yes
16/23 (70%)	Median follow up of 18 months (range 0-201 months)	Nil	Nil	Yes
15/16(94%)	After first infusion at 10 weeks; follow up was extended to 10 weeks after the second infusion	94% immediate diarrhoea, 31% abdominal pain with cramping, 19% belching - resolved within 3 hours. During follow up 3 patients had constipation (19%). 2 patient had infections: one patient with recurrent UTI had UTI	1 hospitalisation for symptomatic choledocholithiasis (unrelated)	Yes
18/20 (90%)	8 weeks follow up for primary response	Mild abdominal discomfort and bloating in 4 patients (20%). One child treated colonoscopically had a transient fever of 38.8 C on day 2 that resolved spontaneously	2 deaths (unrelated), 1 new diagnosis of malignancy (unrelated), 1 hospitalisation for Fournier gangrene (unrelated)	Yes
29/30 (97%)	6 weeks	Nausea in one patient. Nil else	Nil	Yes

CRD criteria			
2. Were patients recruited consecutively?	**3. Were patients recruited prospectively?**	**4. Was loss to follow-up reported or explained?**	**5. Were at least 90% of those included at baseline followed up? Record all possibilities**
yes	Yes	Yes	Y and N 18/19 (95%); one of 19 receiving stool excluded due to missing documentation. 16/19 (84%); a further two did not submit stool sample for primary outcome of c diff toxin testing (determined to be diarrhoea free at 90 days)
yes	yes	no-abtstract	yes
yes	yes	yes	yes

yes	No	No	Not known
yes	No	No	Yes
yes	NO	NO	No FU varied significantly

yes	No	No	Yes
yes	yes	no	yes
yes	No	No	Yes
yes	yes	no loss of follow up	yes 100%

yes	no	yes	yes. 2 patients excluded from final analysis as lost to follow up did not have 12 week follow up data.
yes	Yes	Yes	Yes

yes	no	no loss of follow up	yes
yes	no	no loss of follow up	yes
yes	yes	no loss of follow up	yes
Yes	Yes	no loss of follow up	Yes

yes	no	no loss of follow up	yes
No;retrospective review	No	No loss to follow up	Retrospective review
Yes	no	No loss to follow up	No. Although stated in results that none developed recurrence at 90 days from table patient 12 only followed for 2 months
yes	no	yes	yes

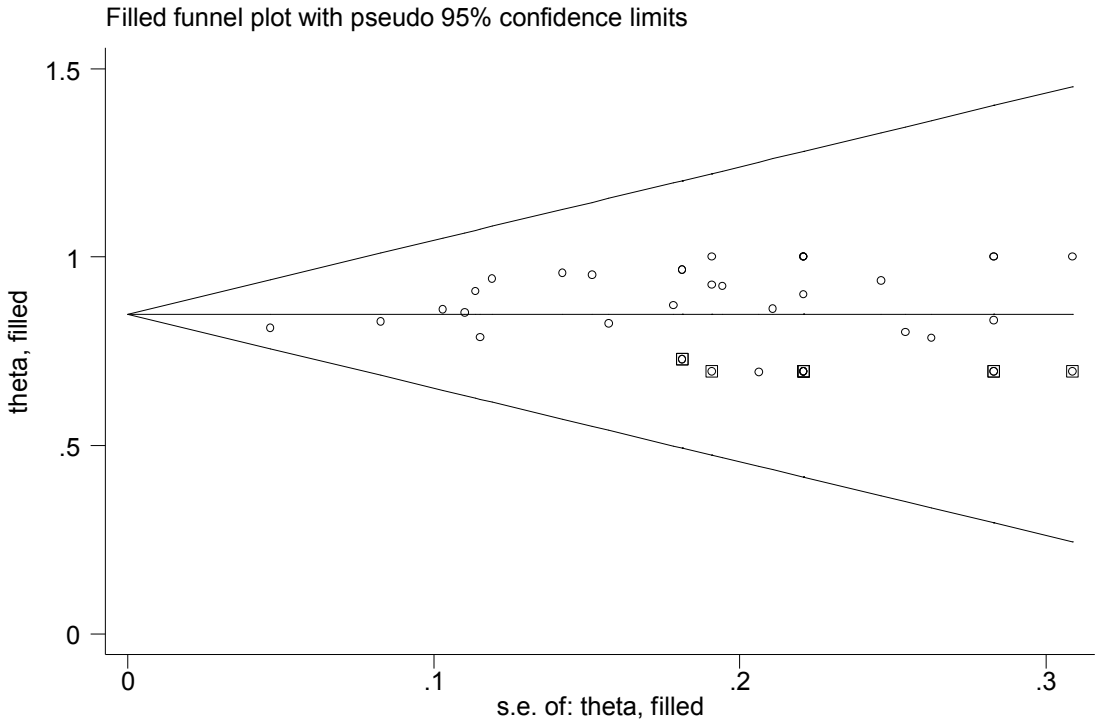
Yes	no	No follow up very variable	yes
Yes	No	No follow up very variable	yes
Yes	No	Yes	Yes
Yes	No	Yes	Yes for 12 weeks
Yes	No	No	No FU varied significantly
Yes	No	No	No FU varied significantly

Yes	Yes	Yes	Yes (100%)
Yes	No	No	Yes
Yes	No	Yes	Retrospective data series based on quesitonares filled by patient or relative
yes	No	No	Doesn't state
Yes	Yes	No	Yes

yes	No	NO	No
Yes	Yes	No	Yes
No	No	No	No
Yes	Yes	Yes, (reported)	Yes
Yes	Yes	None lost to follow up (reported)	Yes
Yes	No	None lost to follow up (reported)	Yes

Supplement 2.Funnel plot of the estimated proportion responding to treatment (ovals) in each included study (y-axis) versus it's standard error (x-axis). Plot includes 'studies' added (crosses) by the Duval and Tweedie nonparametric "trim and fill" method of accounting for small study effects in a random effect meta-analysis model

Case series – multiple infusions



EMBASE - Search strategy

1. exp Clostridium difficile infection/ or exp Clostridium difficile toxin B/ or exp Clostridium difficile toxin A/

2. clostridium difficile.ti,ab.

3. c diff*.ti,ab.

4. (CDAD or RCDI or CDI).ti,ab.

5. pseudomembranous.ti,ab.

6. exp pseudomembranous colitis/

7. (antibiotic* adj2 (diarrhea or diarrhoea or colitis)).ti,ab.

8. (FMT or HPI).ti,ab.

9. ((fecal or faecal or feces or faeces or stool or microbiota) adj2 (transplant* or infus* or transfus* or implant* or instil* or donat* or donor* or reconstitut* or therap* or bacteriotherapy)).ti,ab.

10. (fecal or faecal or feces or faeces or stool or microbiota).ti,ab.

11. transplant*.ti,ab.

12. exp transplantation/

13. 8 or 9

14. 10 and (11 or 12)

15. 13 or 14

16. or/1-7

17. 15 and 16

MEDLINE - Search strategy

1. Clostridium difficile/

2. clostridium difficile.ti,ab.

3. c diff$.ti,ab.

4. Enterocolitis, Pseudomembranous/

5. (antibiotic$ adj2 (diarrhoea or colitis)).ti,ab.

6. (antibiotic$ adj2 (diarrhea or colitis)).ti,ab.

7. pseudomembranous.ti,ab.

8. (CDAD or CDI).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

9. RCDI.ti,ab.

10. Clostridium Infections/

11. FMT.mp. or HPI.ti,ab. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

12. ((fecal or faecal or feces or faeces or stool or microbiota) adj2 (transplant$ or infus$ or transfus$ or implant$ or instil$ or donat$ or donor or reconstitut$ or therap$ or bacteriotherapy)).ti,ab.

13. (fecal or faecal or feces or faeces or stool or microbiota).ti,ab.

14. (transplant$ or infus$ or transfus$ or implant$ or instil$ or donat$ or donor or reconstitut$ or therap$ or bacteriotherapy).ti,ab.

15. Transplantation/

16. Transplants/

17. 11 or 12

18. 14 or 15 or 16

19. 13 and 18

20. 17 or 19

21. or/1-10

22. 20 and 21